MGH News

Vol. 40 No. 1 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS January-February, 1981

Donated Bones of the Dead Resume a Role in Life

Know the Danger of Smoke Inhalation

In terms of peril to human life, whoever said "Where there's smoke, there's fire" more wisely could have warned "Where there's fire, there's smoke."

In the vast majority of blazes that claim lives in the United States each year, officials label smoke inhalation with respiratory damage as the primary cause of death at the fire scene.

Among fire victims who die in a hospital, infection is most often the killer, followed closely by lung damage.

"Most people who perish in burning structures are dead long before the flames reach them," said Jon C. Jones, data analyst at the National Fire Protection Association (N.F.P.A.).

During the November fire which killed 84 persons at the MGM Grand Hotel in Las Vegas, smoke far outraced flames in permeating the tall building.

Smoke delivers a one-two punch. First, it narcotizes the victim by dissipating available oxygen, making him lose his sense of where he is and what is happening. Then toxic gases poison him.

The ingredients of smoke are as varied as the types of substances that can ignite. Deadly carbon monoxide, however, is common to all forms of smoke. Even if this gas fails to kill, it can cause severe neurological defects.

The burning of plastic materials common to virtually every room could fill the air with poisonous fumes from such chemicals as hydrochloric acid, hydrogen chloride, phosgene, and hydrogen cyanide—the latter the same substance used in the executioner's gas chamber.

Polyvinyl chloride (PVC), used in the manufacture of such products as rainwear, garden hoses, phonograph records, and floor tiles, will yield a mixture of 75 different chemical agents when submitted to extreme heat.

During fires, toxins attach to the surface of air-suspended carbon particles whose temperature may range as high as 1,000°C (1,832°F). As the elements are inhaled, they cause constriction of the voice box (larynx), windpipe (trachea), and bronchial tubes,

(Continued on Page 2)

Firefighter struggles to vent burning home of smoke which may contain dozens of toxic substances.

He only followed doctor's orders, but he still wonders whether he inadvertently created a wrong impression.

Some months after William Kennedy underwent major leg surgery at the MGH, the assistant district attorney of Middlesex County appeared in court to prosecute a case. During the proceedings he moved about with the aid of a cane.

When the trial ended, the jury disappointed Mr. Kennedy by acquitting the defendant. Later, one of the jurors approached the defense attorney and remarked, "I wonder if that cane is a prop."

"I guess I carried the cane more than I leaned on it," Mr. Kennedy explained. "I had been told to use the support, but actually my leg felt so good, I didn't really need the stick. Some of the jurors may have gotten the false idea that by having the cane with me I was playing on their sympathies."

The public official was recovering from an operation which represented his only alternative to amputation of his right leg. His problem was a malignant tumor on his shinbone (tibia), just below the knee.

The operation, by a team headed by Dr. Henry J. Mankin, Chief of the MGH Orthopaedic Service, involved removing the cancerous bone and installing in its place a bone from someone who had died.

Transplantations of cadaver bone (allografts) have been performed over many years, but only within the last decade have orthopedists seen much promise in the procedure. Part of the

(Continued on Page 4)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114
Telephone (617) 726-2206

Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD

Charles A. Sanders, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Ralph H. Cluff, Jr., *Typography*

EDITORIAL:

Achieving Their Fullest Capacities

Medicine today suffers from the fragmented image syndrome. The explosion of knowledge which has created super specialists has led to excellent physicians who know a great deal about a narrow area. While this process may focus the attention of physicians on a hand or an eye instead of the patient, the specialist has improved immensely the quality of care.

In reaction to this fragmentation, however, have evolved such movements as holistic medicine. To a degree American medicine can profit from the better aspects of the holistic medicine philosophy without swallowing some of its far-out elements. In fact, though, hospitals have long embraced the idea that medical care means much more than treating a disease. In the mid-19th century, for example, the surgeon who cofounded the MGH gave money to establish the country's first hospital library for patients. This hospital also in the mid-19th century planted the seeds of a volunteer service that visited patients, believed to be one of the first organized hospital-sponsored groups of volunteers in America. Rare is the hospital today which lacks a chaplaincy service to care for the patient's emotional and religious needs. Occupational and recreational therapy are also standard hospital activities.

In 1905 the MGH took a step so revolutionary in its day, so taken for granted today. The establishment of a Social Service Department, the first in any hospital, was eyed with trepidation. Even the physician who then directed the MGH was at first a thoroughgoing skeptic. But it was a farsighted doctor, Richard C. Cabot, who perceived the need. In his own words:

"In the Outpatient Department of Massachusetts General Hospital (and I suppose in most other hospitals) there occurs many times each year a scene not unlike that described in Alice in Wonderland:

' "Have some wine," said the Hatter.

' "I don't see any wine," said Alice.

' "There isn't any," said the Hatter.'

"Without any sense of the humor and pathos of the situation, we say (in substance) to many patients, take a vacation or get a job. There is none in sight and no means of getting any. What do we do then? We pass cheerfully to the next patient."

What emerged from Dr. Cabot's vision was a department whose goal is "to help each patient and the relevant family members to achieve their fullest capacities" in their physical, emotional, and social well-being.

Before too long Dr. Cabot had made the hospital's Director a believer. And today as the MGH Social Service Department looks back on its first 75 years, no hospital of any size and repute would consider an existence without such a department.

Smoke in Airway Weakens Barrier Against Infection

(Continued from Page 1)

producing a wheezing as if the individual were suffering from severe asthma.

Once the foreign bodies enter the lungs, they begin to damage the organs' air sacs (alveoli) which deliver oxygen to blood and receive carbon dioxide from blood for disposal.

Such patients need immediate delivery of 100 percent oxygen to support the cells in the lungs and to help eliminate the acids and gases from the body.

If the patients require intubation rather than a face mask because of a closed air passage, the procedure should be performed with the tube extending through the nose or mouth into the windpipe.

Dr. Noel Gibney, Senior Clinical Fellow in the MGH's Respiratory Intensive Care Unit, emphasized the danger in trying to provide oxygen through a neck incision directly into the windpipe.

"Performing a tracheotomy through a burned patient's skin should be considered only if other methods are clearly unsatisfactory," he warned. "Studies show 90 percent of such patients develop massive infection of the wound."

When a person suffers a charring of the airway, such as from hot carbon in smoke, the effect is the same as if he had burned his hand. The superficial surface which acts as a protective barrier against infection is lost.

In the airway, the lining normally contains cells which are ciliated; that is, they have hairlike projections. These enable one to clear out abnormal secretions and inhaled harmful matter, such as bacteria. Destruction of even a small part of this airway "escalator" would seriously impair the ability of the entire respiratory tract to dispose of health-threatening substances.

In evaluating a patient injured in a fire, physicians quickly look for redness, swelling, or soot in the mouth.

Photographs: Page 1, Robert Patterson; p. 3, courtesy of National Fire Protection Association; pp. 4 (upper), 5, 6, Alan Lucas; p. 4 (lower), Allied Pix; p. 7, MGH Archives; p. 8, Myron Daniels.

Such signs would lead the physician to perform a bronchoscopy, an examination of the major breathing passages using an instrument lighted by a process called fiberoptics.

"Redness of the larynx could be an indication of impending swelling which could close off the airway and asphyxiate the patient," Dr. Gibney said. "Also, many burned patients need administration of fluids which could speed the swelling unless proper measures were taken." A most likely step would be insertion of an oxygen-bearing tube into the windpipe.

Several years ago physicians commonly used steroid drugs to treat inhalation injuries because the medication helped reduce swelling. Subsequent studies, however, have revealed a much higher incidence of pneumonia, blood poisoning (septicemia), and death from infection among steroid-treated burn patients than among burn patients not given such drugs.

Dr. Gibney said that if people were made more aware of the harm that smoke could inflict, there would be a lot less apathy toward such protective devices as smoke detectors.

The United States Fire Administration recently found in a survey that the use of smoke detectors in American households has more than doubled since 1977. However, the survey also showed that a significant number of people were simply not interested in having detectors.

A smoke victim needs immediate oxygen to help clear the lungs.

Mr. Jones of the N.F.P.A. said that, in 1979, 7,780 people died in fires in this country. Of the total, 5,765 (more than 74 percent) were killed by fires in residential properties.

Of the residential fires, the biggest loss of life—4,320 deaths—occurred in one- and two-family homes. Apartment building fires killed 1,180 persons. Fires in hotels, motels, dormitories, and similar housing took 265 lives.

Exact statistics on cause of death probably will never be available because of multiple contributory factors. But fire, health, and safety officials agree that inhalation injuries constitute the principal factor in the majority of the tragedies.

Most residential fires occur at night when occupants are asleep. "People mistakenly think when a smoke detector goes off that they have time to get dressed and pick up valuables before they leave," said Massachusetts Fire Marshal Joseph A. O'Keefe. "Actually,

(Concluded on Page 4)

Surgeon Warned Years Ago of Smoke Perils

"Show me a burn victim with second- and third-degree burns around his nose and mouth from a fire in an enclosed space, and I can guarantee that in nine out of 10 cases he will have respiratory tract damage—and very well may die of it."

When Dr. Anne W. Phillips of the MGH made this statement in 1962, the leading cause of death from fires was considered to be shock, a collapse of blood circulation.

The first woman surgeon to operate at the MGH, Dr. Phillips also was the first to prove through research that lung damage from heat and from smoke inhalation was a primary reason why fire victims died.

Support of this finding came slowly. "By observing closely, we saw so many respiratory complications," Dr. Phillips said, "that the American Burn Association wanted to know at first what we were doing wrong up here in Boston."

Today, with improved methods of controlling circulating blood volume, few fire victims succumb from shock. Lung damage, however, continues to exact a high toll in fires.

Dr. Phillips attributes part of this toll to a lack of concern among many about fire safety.

"They think 'Fire isn't going to happen to me,' " she said. "Yet, a few years ago the National Commission on Fire Prevention and Control heard testimony that during a lifetime every citizen can expect to experience two or three fires, each serious enough to warrant sounding an alarm."

Dr. Phillips is Executive Director of the National Smoke, Fire, and Burn Institute, Inc., a nonprofit organization devoted to educating the public about fire safety.

"It's amazing how many ways people find to get around measures taken for their protection," she said. "They prop open fire doors with a wedge. They paint over sprinkler heads so that no water will come out. They put a penny in a fuse box and destroy the effectiveness of the fuse."

Dr. Phillips admits she is impressed by the response of the American public to suggestions that they install smoke detectors in their homes. She hopes this reflects a more serious attitude about fire safety.

Asked about those who brush aside the idea of using smoke detectors, Dr. Phillips responded, "What can you do to protect people who will not listen?" ■

Cadaver Bone Use Earns High Marks

(Continued from Page 1)

optimism stems from an ability of Dr. Mankin and his staff to preserve live cartilage in conjunction with the donor bone.

Despite his close call, Mr. Kennedy, who is 30, walks without a limp and, for exercise, swims, rides a bicycle, and plays basketball. "I suppose I unconsciously favor the leg," he said in an interview, "but, at the same time, I can feel it getting stronger every day."

Since 1971, Dr. Mankin and his colleagues have performed more than 100 transplantations employing cadaver bone. Although a number of the patients need longer follow-up before the outcome of their surgery can be fully assessed, Dr. Mankin estimated that three quarters of the patients in the entire series had good or excellent results. The main difference is that the "excellent patient" can engage in competitive recreational activities, if desired.

Facing the loss of her left leg because of a bone tumor above the knee, this girl, then 16, had a dead person's bone substituted for the diseased segment. Today, at 21, she is completely well.

Of the remaining individuals who had bone transplantations, fair outcomes far exceeded failures. Fair means the patient no longer had any evidence of a tumor but had limitation of function and needed some kind of brace or other support. Failures denote patients who either required amputation of a limb or died because of recurrent or spreading tumors.

In all instances, no treatment offered as much hope as an allograft. Several patients in the series did not have tumors but conditions such as lost segments of bone resulting from a compound fracture or destruction of part of a joint because of an accident. All are described as doing very well.

Dr. Mankin spoke of a girl who was unable to walk or even stand because a genetic disease called fibrous dysplasia had virtually destroyed one of her thigh bones (femur).

"There was no way to replace her

Smoke Inhalation

(Concluded from Page 3)

they have an average of 42 seconds to get out of the building.

"This is why we emphasize in school fire drills: 'Don't let the children get dressed. Just leave.' "

Michael Shenkman of the N.F.P.A. said that "our organization's position on smoke detectors is that in a residential fire they are the first line of defense."

He said the devices should be installed on each floor of the structure, but at the very least on the ceiling of the hallway outside the bedrooms. The ceiling of the room where most of the household activity takes place deserves next priority.

"Smoke detectors can literally mean the difference between life and death," Mr. Shenkman stressed. "They are so inexpensive today there is no reason not to have them."

Sometimes the question arises over the relative merits of smoke detectors versus heat detectors. The answer lies in how the instrument will be used.

In a kitchen where cooking vapors could accidently trigger a smoke detector, use of a heat sensor would be more appropriate. In general, however, the smoke detector is first choice because the fumes usually travel faster than the heat and would set off an alarm earlier.

Mr. Shenkman emphasized the wisdom of planning.

"Always plan two avenues of escape from each room in the house," he advised. "Designate responsibilities for evacuating small children from rooms. And have a predetermined means of getting down from higher than one-story buildings."

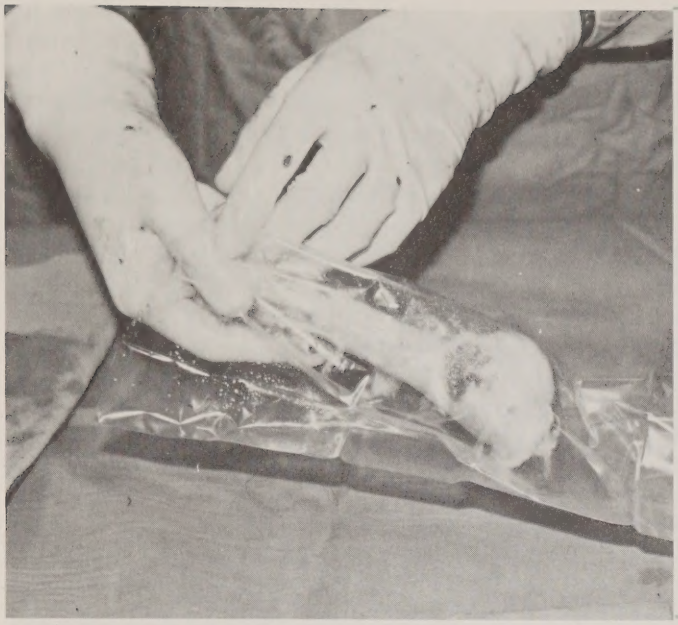
When people awaken during nighttime fires, their first instinct is to jump out of bed and run to a door. A mistake. "They should roll out of bed and crawl across the room," Mr. Shenkman said, "because if they stood up they would risk being overcome by toxic gases."

A hot doorknob usually is a warning of extreme heat on the other side of the door. Try the alternate escape route, i.e. another door or a window.

If one is trapped in a room or faces a risk of straying into a smoke-filled area while escaping, a damp cloth or towel placed over the nose and mouth could markedly reduce the inhalation of smoke particles.

"What escape planning really means," Mr. Shenkman said, "is not having to make any more decisions than one has to in an emergency where seconds are critical." ■

Although wearing breathing support apparatus, these firefighters still needed a respite while battling this smoky fire in Middletown, Pa.



After being immersed in a glycerol solution, this arm bone being prepared for storage is placed in a plastic bag to prevent drying out while frozen. The glycerol preserves the viability of cells in cartilage attached to the bone.

entire femur with mechanical devices," he said, "so we put in an allograft femur as a substitute. The girl is now back at her job."

Surgeons working with bone transplants remain ever alert for complications. Deep infections lead the list of potential difficulties. Also, the allograft can fracture. Experience has shown, however, that the body will accept a cadaver bone.

"The closest thing we've had to a 'rejection,'" Dr. Mankin said, "has been an occasionally long healing process at the sites where the donor bone was joined to the patient's own bone."

On June 3, 1976, in the *New England Journal of Medicine* the MGH team reported on its first group of patients to receive bone allografts. A follow-up report providing detailed statistics on the work to date has been completed for publication in a scientific journal.

One other American medical center, M. D. Anderson Hospital in Houston, also has amassed considerable experience in bone allograft transplantations. Recently, some 10 other institutions embarked on programs of their own, partly as a result of the MGH effort. Abroad, centers in Canada, Sweden, Russia, and Argentina are engaged in bone allograft projects.

Dr. Mankin said the MGH program is being concentrated mainly on tumors because the need in that area is very great. "The work is arduous and complicated," he added, "but if we can prove the efficacy of this system, we will be able to expand our efforts into a whole gamut of orthopedic afflictions."

Bone allografts could substitute for repair bone taken from healthy parts of the patient's own body and for metal fixation devices.

Although the patient's own bone, called an autograft, would heal better than an allograft, the body can spare just so much bone. The size and shape of the material also may not be appropriate, and taking an autograft involves loss of tissue, sometimes a considerable loss.

As for metal devices, Dr. Mankin said that most depend for fixation on materials which are likely to loosen or break as time passes.

In his view, the best designed parts available today for implants are those employed in total hip replacement. "But even they tend to fail in time," he pointed out. "That's why we prefer that the candidate for a total hip replacement be more than 50 years of age. A high percentage of young people ultimately need a second replacement."

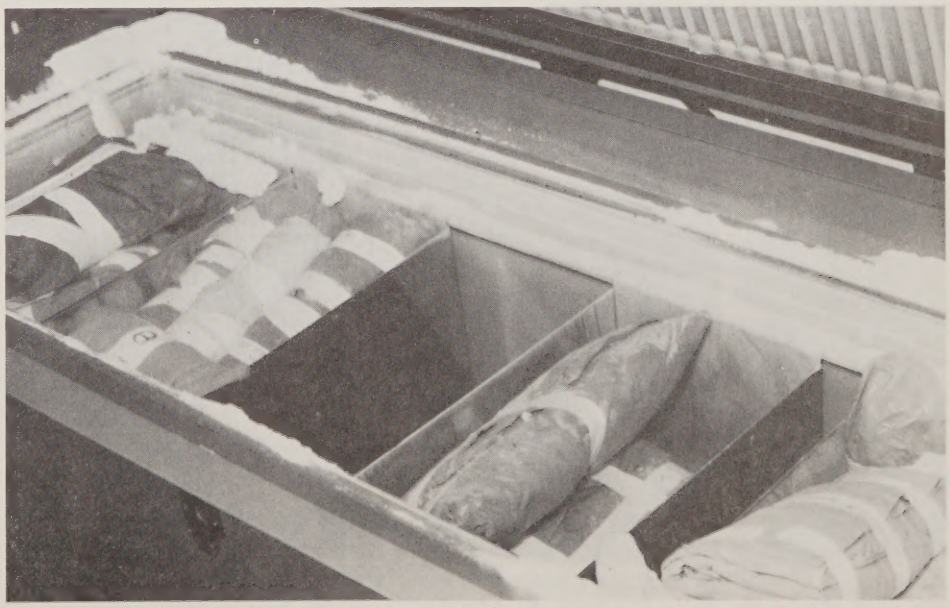
Of critical importance in the bone allograft program is availability of an inventory of donated bone. When Dr. Mankin began his allograft surgical series in 1971, he also inaugurated a bone bank at the MGH. Now containing some 200 bones of various kinds, the bank is directed by Dr. William W. Tomford, former Chief of the United States Navy Tissue Bank at Bethesda, Md.

Very strict criteria govern selection of cadaver bone for deposit in the bank. The bone must be retrieved within 12 hours after the donor's death. The donor must be more than 15 years of age (to ensure closure of growth plates in the bone) and under 45 (to decrease the likelihood of bone-thinning or arthritic processes).

The donor's history must be explored to exclude major metabolic diseases, tumors, infections, etc. If the prospective donor has been on high-dose corticosteroid drugs or on a respirator for longer than a week, the donor would probably be rejected.

In all instances, permission to obtain bone must be secured either as a bequest from the donor made prior to death or from next of kin.

(Concluded on Page 6)



Freezer holding donor bones was custom made with compartments to permit easy retrieval of any particular type of needed bone.

Central Bone Bank Could Speed Repair

(Concluded from Page 5)

Three major bone banks operate in the United States. In addition to the Navy's facility at Bethesda, centers with close to a thousand bone parts each are situated at the University of Miami and in San Francisco. A number of small bone banks also exist, but some have only crushed bone to help with problems such as spinal fusions or compound fractures.

"We would like to see the establishment of centralized bone banks," said Dr. Tomford. "Storage in such centers would allow more rapid procurement of an appropriately sized allograft for a waiting recipient. Lack of a good inventory limits the surgeon's efforts to make the best possible repair."

Dr. Tomford, an Instructor in Orthopaedic Surgery at Harvard Medical School, added that it is not economically feasible for many hospitals to operate their own bone bank.

In 1979, for example, costs for running the MGH Bone Bank were more than $50,000. Six surgeons utilized a total of 22 allografts from the bank. On the basis of the individual bones used, the expense exceeded $2,000 per implant.

If a limb were amputated, however, and replaced by a prosthesis, the cost would range between $1,000 and $2,000 for an artificial leg and anywhere from $600 to $4,500 for an arm, depending on the sophistication built in.

Dr. Mankin pointed out that regardless of the amount of technology employed, no device would make up fully for the capabilities and aesthetic appearance of a natural limb.

In the past few months the MGH Orthopaedic Service has received four or five requests from hospitals for guidelines on how to bank bone.

One of the keys to the MGH success has been the preservation of cartilage in a live state even though kept frozen at minus 80°C (minus 112°F) together with bone and attached tendons and ligaments.

Dr. Mankin, who is also Edith M. Ashley Professor of Orthopaedic Surgery at Harvard Medical School, said that, unlike the other materials, the cartilage must be live because its cells must be able to reinforce the framework (matrix) of the donor cartilage. Otherwise, the cartilage may deteriorate.

Studies by Drs. Mankin and Tomford showed that immersion of cartilage in a preservative solution containing glycerol or dimethyl sulfoxide (DMSO) could maintain viability of the cells during the freezing and thawing processes.

The glycerol treatment is similar to a process described some years ago by Dr. Charles E. Huggins, Director of the MGH Blood Transfusion Service, for long-term storage of blood.

Bones from the MGH bank have been used successfully after having been stored for as long as five years. "As far as we can tell, there is little deterioration if you store the donor bone for up to 5 to 10 years at minus 80° centigrade," Dr. Tomford said, "but if you intended to keep it frozen for a very long time, you'd need a lower temperature."

Dr. Mankin's department treats well over 150 tumor patients a year. The majority can be cared for by traditional methods. To ensure the safest margin for the patient's recovery, Dr. Mankin also restricts allograft candidates to those with low-grade malignancies.

A large percentage of the transplantations at the MGH thus far has involved giant cell tumors and chondrosarcomas. The first is a rare cancer which usually destroys a bone near a knee or a wrist and sometimes spreads into a joint. The second is a cancer arising from cartilage cells.

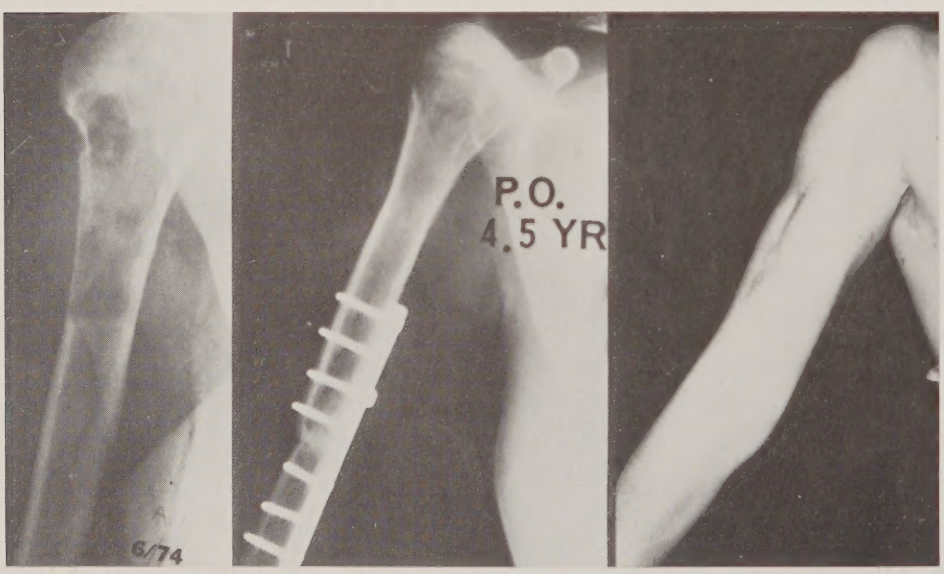
The size of the tumor often determines how normal the affected limb will be after surgery. The larger the tumor the more bone, muscle, ligaments, tendons, and nerves will have to be removed to ensure elimination of the tumor.

Experience has taught MGH surgeons that if the surgery necessary to remove the tumor is likely to result in sloughing of skin, the outcome is apt to be poor and hence such patients are not considered good candidates for the procedure.

In addition, Dr. Mankin will not perform such surgery on a patient undergoing drug treatment (chemotherapy). All tissue becomes "sick" under this treatment, but healthy tissue only temporarily. The fastest growing tissue, the cancer, becomes sickest and dies. Since allografts, however, *require* a rapid growth of cells to bridge the space between the graft and the patient's bone, chemotherapy, when given simultaneously, tends to seriously retard healing.

Dr. Mankin is thinking of devising a metallic spacer which could substitute for a diseased bone. The patient could then receive chemotherapy and after a year, if conditions were suitable, the drug could be stopped and the allograft inserted.

With safeguards such as this in patient care and a program of continued aggressive research, Dr. Mankin believes that allograft transplantations may one day become a major tool in managing many kinds of bone disorders, not only life- or limb-threatening tumors. ■



X ray at left shows cancerous right upper arm bone of a 19-year-old girl. Center X ray and right photo were taken 4½ years after surgeons replaced the diseased bone with cadaver bone.

Miss Ida M. Cannon, first MGH Chief of Social Service, and Dr. Richard C. Cabot, originator of the department.

Medical Social Work Passes 75th Year

In June 1905, a courageous MGH physician dared to assert that the hospital lacked a certain something in its care of patients.

Dr. Richard C. Cabot, who served in the Outpatient Department, wrote several friends that of 500 patients who visited the MGH clinics daily at least 50 were sick because of some quality missing in their lives, rather than from any germs, poisons, or accidents.

The doctor perceived that the time needed to examine the hundreds of patients made it nigh impossible to delve also into a person's home life, work responsibilities, or worries. Yet, he pointed out, such considerations were often essential to sound medical care.

Dr. Cabot sought to fill the void at the hospital by creating the post of social worker, supported by private contributions. His letter solicited qualified nominees.

On October 1, 1905, a desk appeared opposite a lunch counter in the corridor of the Outpatient Department, and the first social service unit in any hospital came into being.

Instead of being viewed largely as an organic problem detectable through physical examination and laboratory tests, disease took on a broader meaning. It became apparent to all that the emotional and social aspects of illness also had to be understood and dealt with if medical treatment was to be truly effective.

Social service so clearly demonstrated its worth at the MGH that even before the department's probationary period ended other medical institutions were seeeking advice on establishing similar units.

Looking back 75 years to the pioneering efforts of a tiny handful of social workers, the MGH prides itself today on a social service staff of nearly 114 people, including 55 with master's degrees in social work, 30 case work assistants, and seven registered nurses. During fiscal 1980, the department screened or provided services to 39,026 patients.

"Our goals today are exactly the same as those outlined by Dr. Cabot," said Miss Eleanor Clark, Director of the Social Service Department for the past 16 years. "Our responsibility is to assist the patient in making the best use of medical care, whether it be preventive, curative, or rehabilitative."

The problem solving confronting the medical social worker generally falls into two broad categories: 1. dealing with the patient's fears which may involve his illness, job status, future lifestyle, and family relationship; 2. seeing to it that the patient has access to needed community resources.

"There is a resource for virtually anything that any patient may need," Miss Clark said, but she added, "Sometimes it almost takes a Ph.D. to learn where the resource is and how to work out the procedure necessary to get the patient into the system."

Many of the patients for whom social workers fill roles as advocates in the community are inarticulate, old, or frail. As Miss Clark put it, "They simply don't have the capacity to find their own way through that intricate system or nonsystem that exists out in the field."

Miss Grace K. Nicholls, Associate Director of the MGH Social Service Department, emphasized the qualities sought in prospective staff members, aside from formal academic training: "You're really looking for people who can be sensitive to the patient's response to illness and stress, and who at the same time can be innovative and effective in helping the individual."

The three precepts upon which the MGH was built—patient care, education, and research—have guided the growth of the Social Service Department.

During its formative years, its involvement expanded rapidly to include the Neurological, Children's, Orthopaedic and Nerve, and Genitourinary clinics. By 1914, social service also had become available to patients in the wards.

Miss Ida M. Cannon, who from 1907 had served as "head worker," became Chief of Social Service in 1914. She held the position until her retirement in 1945.

When she stepped down, the MGH Trustees adopted a resolution saying that while Dr. Richard Cabot was the founder of medical social work, "Miss Cannon was in large measure the instrument who through the years put into operation the principles and developed the techniques of this essential service. A large part of the credit for the development of medical social service here and in other hospitals is due to her."

A 19-year member of the MGH department took the helm when Miss Cannon retired. Except for leave to serve as Chief of Social Service in the Mediterranean Theatre of Operations in World War II, Miss Josephine Barbour supervised steady growth of the department until 1964 when Miss Clark succeeded her. Only three people have directed social service in 66 years.

In order to have staff members as close as possible to the patients they serve, social service offices are set up

(Concluded on Page 8)

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114
Address Correction Requested

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Foster Homes Provide Care for Elderly

(Concluded from Page 7)

throughout the 1,082-bed area at the MGH as well as at the MGH-Chelsea Unit and the MGH-Bunker Hill Health Center in Boston's Charlestown district.

In addition to individual counseling, social workers often lead group meetings with patients and family members to discuss questions of common concern. Sometimes staff nurses will participate, such as when patients who have undergone heart surgery get together to talk about their anxieties and seek medical advice.

Miss Clark and Miss Nicholls meet regularly with unit supervisors to discuss particularly difficult patient care problems, as well as overall issues affecting the department.

In 1964, Miss Clark initiated what is believed to be the nation's first hospital Transfer Office. Now called the Continuing Care Planning Unit, its responsibility is to assist patients in finding suitable long-term care facilities to follow hospital discharge. Nurses assigned to the unit consult with the physician and social worker attending each patient to assess his needs.

Because of the success of the MGH unit, Massachusetts today requires the same kind of service by every hospital in the state.

In 1978, Miss Clark and her staff inaugurated a Family Care Program to provide foster homes for elderly or frail patients who require continuing assistance, but not necessarily at the comparatively high cost of a nursing home.

To date, the program has placed 47 patients. Several months ago, the government approved Medicaid participation.

On occasion, irrational behavior on the part of an elderly patient jeopardizes a foster home arrangement or other form of community-based care. Plans are being made with the MGH Psychiatric Service to study such dilemmas and evolve ways of overcoming them. "There are many forms of elderly behavior that resemble dementia but which are, in fact, reversible," Miss Clark pointed out.

MGH's foster home program reduces patient's dependence on institutions while assuring continuation of needed care at less expense.

Social service has frequently become a partner in interdisciplinary projects at the hospital. As long ago as 1911, the department assisted in probing social and industrial conditions affecting working girls.

In 1913, social workers joined in studying 147 cases of lead poisoning. In later years, they sought to learn the reactions of patients to a diagnosis of cancer and how help could be offered.

Education has always been a key facet of the MGH social service operation. Seventy years ago the then fledgling department became affiliated with the Boston School of Social Work (now a part of Simmons College) and provided students with opportunities to train at the hospital.

Today, in addition to Simmons, the department offers experience for master's degree candidates from Smith College and Boston College and collaborates in the training of social work assistants at Middlesex County Community College in Bedford, Mass.

In addition, the department works closely with the newly inaugurated MGH Institute of Health Professions (formerly the Education Division) in offering a 12-month course leading to a certificate in social work.

Miss Clark and Miss Nicholls serve on the faculties of the MGH Institute, Simmons College, and Smith College.

The department has collaborated for many years with both the Massachusetts and American Hospital Associations on matters involving social work.

A two-day program commemorating the 75th anniversary of medical social work at the MGH is being planned. In addition to a reception, the program will include a series of workshops dealing with some of the most important issues prevailing in the field.

The coming sessions underscore a long-recognized fact: that competence in any profession requires continuous learning. ■

MGH News

Vol. 40 No. 2 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS March, 1981

Responding to the Specific Blood Needs of Patients

When Does Grief Become Abnormal?

At some point in everyone's life, whether it be happy or sad, rich or poor, full or empty, death intervenes. It is an inevitable part of living. And with death, there arises the most painful of emotions: grief.

Although there is no explanation why some people die "before their time" while others go on, society makes provisions for the grieving process. Soon, most mourners adjust to the environment in which the deceased is missing and resume the normal course of their own lives.

Some mourners, however, with particularly close and emotionally complicated ties to the dead person, are unable to adjust on their own. They need help to resolve their grief.

"Time can seem to stand still for these people," said Dr. Aaron Lazare, Director of MGH Outpatient Psychiatry and Deputy Chief of the hospital's Psychiatric Service. "Without professional aid, they may remain grief-stricken for years, even a lifetime."

To understand unresolved grief, one must know what constitutes normal sorrow.

In normal grief, the human mind refuses full-scale acceptance at first that a loved one has died. "I can't believe it. It's impossible," the survivor insists. The denial acts as a shield against the heavy assault of the truth.

(Continued on Page 2)

Incoming Chief Sees Need to Emphasize Spirit of Oneness

America stands poised on the threshold of a revolution in biology, rivaling perhaps the impact upon society of the Industrial Revolution.

Laboratories are already making rare compounds to augment bodily substances such as insulin for the control of diabetes and potentially cancer-fighting interferon.

The possibility of regulating birth defects traceable to malfunctioning genes no longer seems merely a pipe dream.

"To be meaningful, such achievements require more than the dedication, skill, and insight of the research-

(Continued on Page 5)

Technician George Jones prepares to add glycerol to red blood cells so they can be frozen for storage until needed.

In these days when the turbulent economy strains the purse strings of Americans, the most precious gift in life has never been a better bargain.

A donation of a pint of blood, once calculated to serve one patient, now benefits two or more.

This has resulted from revolutionary changes in blood banking. Whole blood is no longer the mainstay of inventories at major banks. Instead, they separate the blood into its basic components. In this way, with the same exactness that a druggist fills a prescription, the blood banks can provide just those blood factors which a patient actually requires.

No less important is an ability through special freezing techniques to preserve the most frequently used factors, red cells and plasma.

At the MGH, red cells which carry oxygen from the lungs to all parts of the body have been used successfully after being frozen for 11½ years.

Dr. Charles E. Huggins, Director of the hospital's Blood Transfusion Service, pioneered a practical way to freeze blood by using glycerol to maintain the viability of the cells.

Dr. Huggins said that the shift in blood banking emphasis from whole blood to separate stocks of red cells, white cells which fight infection, plasma to replenish blood volume, and platelets for proper blood clotting has gone far toward a more efficient use of blood.

In the past, as much as a third of all blood donated in this country for transfusions offered no benefit. High among the reasons was the fact that whole blood reserved for emergencies

(Continued on Page 4)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114
Telephone (617) 726-2206

Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD

Charles A. Sanders, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Ralph H. Cluff, Jr., *Typography*

EDITORIAL:

An Extraordinary Beginning

Nations from time to time need to renew themselves. Democratic countries achieve this by rallying around causes like the Iran hostage crisis, through elections, and by a variety of other means. Institutions too employ a number of methods.

Through the years the MGH has periodically been infused with new life. The hospital began with a bang, when the second President of the United States presided over the first corporation meeting. An early example of infusion was the demonstration to the world in 1846 of surgical anesthesia. Sometimes the infusion has come in the form of a dramatic event like that, sometimes in the shape of a major new building, on other occasions in the guise of a towering leader.

Last month the MGH announced a $114 million fund-raising campaign. It embraces the regeneration of old patient-care buildings, the replacement of outmoded ones, the construction of a new research structure, and funds to complete the financing of new buildings and to fill the needs of the MGH Institute of Health Professions and the hospital's Treadwell Medical Library. Clearly this represents the most massive undertaking in the hospital's 170-year-old history.

To achieve its ends, the MGH could have pursued a recent trend in American hospitals: borrowing money. Such a course, however, would have forced tomorrow's patients to pay for today's needs. The result? Sharp patient-care cost increases to pay back decades of high interest bonds. Instead the hospital chose to follow its tradition of turning to its friends in time of need. Already these friends have responded with more than $31 million in pledges. A $15 million pledge from Arthur O. and Gullan M. Wellman of Florida, for example, will result in a desperately needed Wellman Research Building. An extraordinary beginning toward the fulfillment of an extraordinary need.

Grief That Persists Beyond Six Months May Need Therapy

(Continued from Page 1)

Then follows an outburst of tearfulness and restlessness alternating with numbness or frozen withdrawal lasting up to a couple of weeks.

As full realization of the loss sets in, the bereaved develops other kinds of bodily symptoms: a tightness of the throat, a shortness of breath, a need for sighing, an empty feeling in the pit of the stomach, and muscular weakness.

Even though the bereaved may have had infrequent contact with the deceased, the survivor's mind fills with thoughts of the person who died. Even his mannerisms, such as a limp or complaints of the same kind of pain, may be adopted.

The bereavement may be expressed in terms of anger: "How could he have left me alone?" Or in terms of self-blame: "If only I had been driving the car. . ."

Religious customs wisely provide for friends and family to gather and talk about the dead person. "Tell me. How did it happen?" the mourners are asked. They go through the story not once but a number of times.

"You wonder how they can stand it," Dr. Lazare said, "but actually it is a healthy part of the grief process. By reviewing in detail how they put the dead to rest, so to speak, they manage to get the heavy feeling out of their hearts."

Uncomplicated grief causes minimal disruption of normal functioning. Absence from work may range from only a few days to two weeks. Usually, the grieving process runs its course within six months.

Beyond that period, evidence of unresolved grief might include:

Continuation of depression that began with the death, more symptoms of self-reproach and guilt, an unconscious search for the lost person, a feeling that the death occurred only yesterday, unwillingness to move belongings of the deceased, diminished participation in religious activities and other rituals,

Photographs: Page 3 (upper), courtesy of McLean Hospital; p. 8, Robert Crivello; all others, Myron Daniels.

and inability to discuss the deceased without crying or the voice cracking.

Dr. Lazare estimated that unresolved grief constitutes an important aspect of the problem in about 15 percent of the patients he and his colleagues treat in a general outpatient practice.

The specific treatment techniques are complex and vary from one patient to another, but the goal is the same. It is to help the patient accomplish what he could not do immediately after the death, the cognitive and affective work of mourning.

At some point in the series of doctor-patient meetings, the patient's voice may crack. His facial muscles may quiver. And his eyes may water and turn toward the therapist. "This is a critical moment," Dr. Lazare emphasized, "for the patient is asking the clinician to tolerate and support the crying and the entire process of mourning."

When it seems appropriate, the doctor will suggest what should be done, perhaps a visit to the cemetery or a frank talk with friends or relatives about the departed loved one. "In spite of this directive approach," Dr. Lazare cautioned, "the clinician must not impose upon the patient any predetermined timetable for 'a cure.' "

It is not unusual for people in certain circumstances to endure prolonged grief. For example, friends who would be supportive following the death of a parent, sibling, or child might not offer the same support following other losses such as miscarriages or abortions.

Dr. Aaron Lazare lectures on grief.

Time can seem to stand still for some grief-stricken people unless they receive help to readjust. (Posed photograph).

There are those who suffer so-called unspeakable losses: The homosexual who cannot admit his closeness to someone who died. The woman who had an affair with a married man who died. The person whose loved one succumbed from an overdose of an illicit drug.

What about the socially isolated? Dr. Lazare told of a college coed who lost a close relative but was not informed of the death immediately because the student was in the midst of exams. By the time she received the news, everybody else had already gotten over the shock. The student became so distraught she required psychotherapy.

The person who is the strong one in the family often becomes shortchanged. Since he must handle all the funeral arrangements, he cannot allow himself to be weak. Thus, he may be unable to participate adequately in the mourning process.

Dr. Lazare, who is also Associate Professor of Psychiatry at Harvard Medical School, said some people strive to avoid grieving because their feelings toward the deceased include both love and hate.

"They do not want to remember the hate because it would only make them feel terrible, so they try to erase the entire picture from their minds," he said.

"In seeking to help these people, I think we can assure them that they would not be so miserable over a loss unless a lot of love was also present.

"The more a person can make peace with his negative feelings the easier the grieving will be."

Dr. Lazare warned that if a mourner does not reconcile with unfortunate experiences of the past the alternative could be a painful reminder in the future.

He told of a woman who suffered a miscarriage after eight months of pregnancy. The woman nearly hemorrhaged to death and became enraged at the unborn child. Later, she again became pregnant, had a baby, and gave it the same name that had been chosen for the first. She found, however, that she could not talk to the infant, or relate to it in any way.

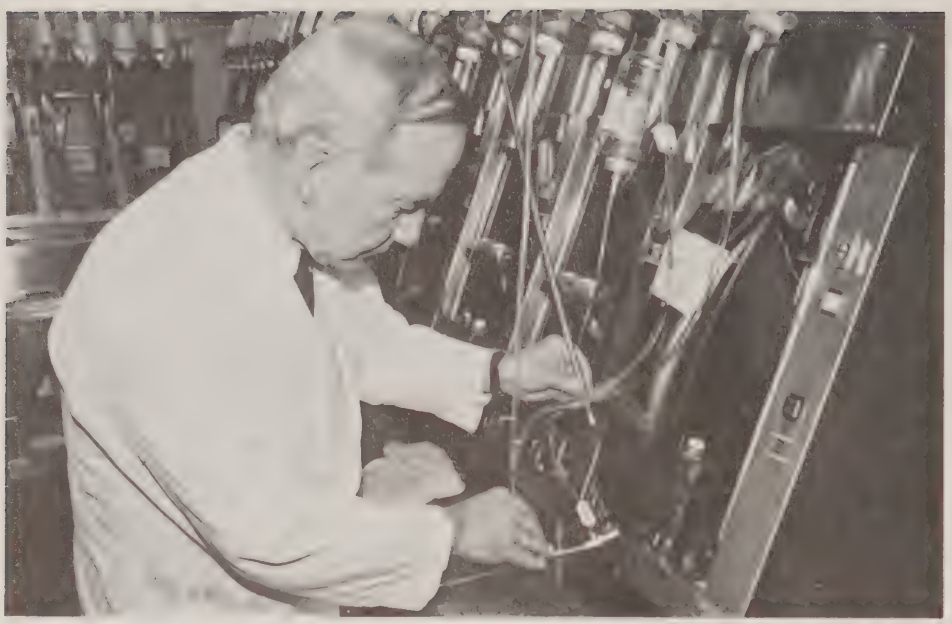
Not until after the mother had dealt with all the miserable feelings she had about the miscarriage was she able to adopt a positive attitude toward her child.

If there is one thing a bereaved person should never be told, it is, "You'll get over it."

" 'To get over it' implies that the loved one who died is no longer a part of the life of the bereaved," the doctor explained. "One never gets over such a loss, but one can make peace with it and resume a meaningful life of one's own."

Dr. Lazare added that no extraordinary skills are needed to help a person deal with so-called normal, or uncomplicated, grief.

"The principal requirements," he said, "are a good heart, a good ear, and a sense of kindness and compassion." ■



Dr. Charles E. Huggins checks on removal of glycerol from red blood cells which have been thawed for patient use.

Components Raise Blood Bank Efficiency

(Continued from Page 1)

during certain operations often became outdated.

Some years ago when the MGH primarily transfused whole blood, it was not uncommon for eight percent of a year's donated pints, or units, to become outdated; and because of freezing blood the MGH had one of the best efficiency records anywhere. With the switch to blood components, the percentage of unusable blood has fallen to less than one-tenth of one percent.

Each day, the Blood Transfusion Service processes between 100 and 125 units of donated blood to meet the hospital's immediate needs and to maintain adequate reserves. Only five percent of the daily supply is retained as whole blood. Certain procedures, especially cardiac surgery, mandate the availability of fresh whole blood.

The remainder of the day's donations is fractionated in fast-spinning centrifuges within minutes after being collected.

Technicians refrigerate 60 percent of the red cells at temperatures between 1°C and 6°C (33.8°F and 42.8°F). To facilitate infusion when the time comes, the cells are suspended in a small quantity of plasma. No attempt is made to exclude white cells (which number one in every 900 reds).

The red cells that are left are combined with protective glycerol and frozen at minus 85°C (minus 120°F).

To assure freshness, the MGH uses only plasma that has been frozen. Platelets and white cells, however, cannot be preserved that readily.

"We refrigerate platelets with good results," Dr. Huggins said, "but we cannot freeze them. We would lose about half if we did."

For optimal effect platelets must be administered within three days. Therefore, blood collected during holiday periods is essential for platelet gathering.

As for white cells, they must be transfused within 12 to 24 hours after collection, and they are usually kept at room temperature.

Thanks to a procedure called leukapheresis (*MGH News,* May 1977), white cells can be separated from a donor's blood even as it is being given. However, instead of the 10 to 15 minutes required to donate a pint of blood, isolation of the white cells alone may take up to three hours.

Dr. Katharine Kosinski, an Assistant Medical Director of the Blood Transfusion Service, said one can appreciate the value of administering blood components instead of whole blood by considering the plight of leukemia patients:

"As time passes, their blood requirements often change. They might need white cells at one point, platelets just a short time later, and then, perhaps, red cells. If you tried to fill the bill each time with whole blood alone, you would not be giving the most effective component, and you would run the risk of volume-overloading the patient."

Then, too, the problem of inefficient use crops up again. Why give a patient an element of blood he does not need when the same factor might prove lifesaving for someone else?

For example, patients with inherited bleeding disorders are often helped by a special preparation made from donated blood containing high levels of an antihemophilic factor.

Recently, a middle-aged patient with blood coagulation problems underwent surgery at the MGH for a procedure in which surgeons bypassed two obstructed heart arteries and replaced a heart valve (aortic). He received a total of 60 units of the antihemophilic preparation before, during, and after the operation. His tendency to bleed remained well controlled.

Another benefit of components is their wider application than whole blood. A patient with type B blood, for example, can accept only type B whole blood. On the other hand, if he were given red cells alone, type B or O could be selected. Type B or AB plasma could be given. Platelets could come from any blood group.

In addition to typing blood components under the so-called ABO formula, technicians determine the Rh factor. Although this is found on the surface of red cells, plasma and platelets must also be checked because a few red cells may linger in these products.

Some institutions criticize supporters of blood components as being overzealous. These centers feel obliged to stock sizable quantities of whole blood because of the possibility of emergencies involving massive bleeding.

Dr. Huggins said components can deal effectively with such critical situations.

"There is usefulness for whole blood, of course," Dr. Huggins remarked, "but in the routine operation of a hospital, it is vastly more efficient to use packed red cells, plasma, and platelets."

Doctors see a valid exception to these guidelines when patients need blood during certain types of surgery. Researchers have developed operating room techniques which make possible reuse of the patient's own blood (*MGH News,* October 1974).

One procedure, called hemodilution, provides for infusing the patient with a salt or protein solution until major bleeding from the surgery is controlled. Then, the patient receives blood taken from him just before the operation

Spirit of Unity Speeds Problem Solving

(Continued from Page 1)

er," said Dr. John T. Potts, Jr., who on May 1 will become Chief of Medical Services at the MGH. "The role of the physician treating the patient is equally crucial. The practitioner, after all, presents the challenge to the investigator and determines whether the proposed solution works."

Dr. Potts said that the deep sense of mutual purpose and mutual appreciation that has existed for generations between researchers and clinicians at the MGH helped the institution earn the high esteem it enjoys today. But he describes the long tradition of close collegiality as endangered:

"Medical practice and research have become extraordinarily complex. The Department of Medicine is vastly larger than in 1957 when I began training here as a Resident. Difficulties that size imposes on personal communication and especially the impact of ever increasing state and federal regulations governing reimbursement and health policy have introduced elements which naturally tend to dampen enthusiasm."

Presently winding down the duties he has held since 1968 as Chief of the hospital's Endocrine Unit, Dr. Potts said his primary goal in his new post will be to reemphasize and rekindle a spirit of oneness in a continuing pursuit of excellence in patient care, education, and research.

"If you didn't know the character of the staff people working at the MGH, you would think at first glance that many were merely effective but compulsive workaholics," he said, "but the fact is that what these talented researchers and practitioners do, they do with devotion and zeal. Such people should enjoy one another's presence and the diversity of what is going on here."

The list of accomplishments facilitated by the unusually close ties between the prober and the patient care giver runs long.

At one time, for example, physicians treating patients for severe heart failure were hard pressed to assess the precise effects of digitalis, used to strengthen the contraction of the heart. A research team headed by Dr. Edgar Haber responded by developing the first test (immunoassay) to measure the circulating levels of the drug, one of the most frequently used medications.

As an extension of that, the Haber group also developed antibodies to fight digitalis so that if a patient were found to be suffering from severe digitalis intoxication the drug's excessive effects could be reversed.

The referral to MGH specialists of patients with particularly difficult problems thus led to laboratory solutions which the specialists could apply to the people they were caring for. In many instances, the physicians wear two hats, that of the care giver and that of the researcher.

Despite an extensive background in research which earned him an international reputation as an authority on calcium metabolism and the hormonal mechanisms that govern it, Dr. Potts has always devoted time to patient care as well. He intends to continue his practice and will also serve as James Jackson Professor of Medicine at Harvard Medical School, a chair honoring a cofounder of the MGH and its first physician.

The new 49-year-old Chief of Medicine will also continue to pursue endocrine research, but because of the limits on his time, he has named a successor as Chief of the Endocrine Unit.

"I've chosen Dr. Michael Rosenblatt, a member of our endocrine research staff who is now also in charge of the Endocrine Associates outpatient group," Dr. Potts said. "He is an excellent physician and one of our leading basic investigators with a broad sense of biologic understanding. He brings considerable leadership ability and personal warmth to his new post."

Dr. Rosenblatt graduated summa cum laude from Columbia College in 1969 and magna cum laude from Harvard Medical School in 1973. He ob-

(Continued on Page 6)

---

began.

Another technique, known as intraoperative autotransfusion, employs a special machine to retrieve blood lost during surgery. The machine then pumps it back into the patient.

In another blood conservation measure, researchers have worked out a way to rejuvenate red cells which have lost their oxygen-carrying capacity while in storage. Dr. Huggins described the technique as somewhat complex, however, and added that through its very effective blood management program the MGH avoids the problem of having to upgrade cell function.

"We take an inventory four times a week of every drop of blood we have," he said. "We check to see what has been distributed and what the age is of the remaining supplies. In this way, we can judge, well in advance of outdating, whether we have too much of any particular blood type. If so, we can freeze the excess."

Because of scrutiny of the nonfrozen blood in stock, 75 percent of all transfusions at the MGH involve blood donated the same week. Twenty percent draw on blood collected the previous week, and five percent employ blood in its third week of shelf life.

The MGH mandates that no patient may receive during any 24-hour period more than one unit of blood in its third week.

Dr. Huggins views a definite trend throughout the country toward the use of components.

"I remember a patient who suffered very serious burns," he said. "Over a period of several months in the hospital, the patient, who was in his early 20s, received 178 units of frozen red cells, 586 units of fresh frozen plasma, and 10 units of platelets. He made a splendid recovery.

"One can cite instance after instance in which the use of components proved lifesaving to the patient." ■

Technician Susan Flagg retrieves red blood cells from refrigerator where they can be preserved for up to 21 days.

Training Program Draws Top Talent

(Continued from Page 5)

tained his postdoctoral training at the MGH.

Now an Assistant Professor of Medicine at Harvard Medical School, he has authored numerous scientific papers, most of them dealing with studies of parathyroid hormone (PTH).

An author of more than 300 scientific publications, Dr. Potts developed at the MGH what fellow professionals describe as the most versatile, productive, and broad-ranging research unit in calcium and bone metabolism in the world.

The unit's training program has attracted highly talented people not only from throughout the United States but also from such countries as France, England, Ireland, Switzerland, Japan, China, Australia, New Zealand, Venezuela, The Netherlands, and Canada.

Graduated maxima cum laude from LaSalle College, Philadelphia, in 1953, and the University of Pennsylvania Medical School in 1957, Dr. Potts trained at the MGH until 1959 when he joined the National Heart Institute.

There, he worked on PTH and related issues until 1968 when he returned to the MGH to head its Endocrine Unit. Several members of his research team joined him in the transfer.

In their PTH studies at the Heart Institute and the MGH, Dr. Potts and his coworkers developed a major series of advances in knowledge of the chemical properties and biological role of the hormone, including practical applications for its use in diagnosis.

In addition to sharpening the diagnosis of disorders involving the parathyroid glands (*MGH News,* September 1980), Dr. Potts and his team are conducting trials to learn more about the basis for calcium deficiency in the elderly.

In one series, the investigators are giving such patients PTH to try to learn whether an inadequate production of vitamin D is contributing to their problem.

In other trials, small doses of PTH in combination with agents such as vitamin D are being used to try to reverse bone loss in patients with osteoporosis (*MGH News,* October 1980).

Preliminary results suggest the approaches are promising in understanding the cause and improving the treatment of osteoporosis.

Studies conducted by the Potts team made possible the manufacture (synthesis) of salmon calcitonin, a hormone subsequently introduced worldwide for the treatment of Paget's disease, an affliction which deforms bone and leaves it structurally weak (*MGH News,* April 1976).

Recently, Dr. Potts and his coworkers have adopted recombinant DNA techniques to study how thyroid and parathyroid tissue regulate the manufacture of calcitonin and PTH, respectively, in normal and diseased states (*MGH News,* September 1980).

The work to increase knowledge about the structure of the genes for these hormones and control of their activity is coupled with efforts to produce the hormones artificially in bacteria and cell cultures, as is being done by other laboratories with interferon and insulin.

The training program in endocrinology instituted by Dr. Potts attracts nationwide attention because of its unusual structure. Five autonomous MGH units—thyroid, diabetes, endocrine, molecular endocrine, and reproductive endocrine (gynecology)—voluntarily integrate much of their efforts in patient care, teaching, and research. Trainees thereby receive not only an unusual breadth of knowledge but also unique opportunities to decide on future specialization.

Speaking of the hospital in general, Dr. Potts said that "year after year we fashion house staffs from among the brightest, most hard-working, and most dedicated young doctors around, but although they benefit greatly from their presence here, are they missing anything?

"I'm very anxious to experiment with new ways of sharing the richness of the institution with the house officers. I want to assure them not only the very best medical education but also guidance along career paths."

Recent house staffs have included increasing numbers of young women MDs. "I think that in gauging career opportunities some of these women need more role models at the staff level," Dr. Potts stated, and he added: "We are watching carefully for the opportunity to appoint more deserving women to staff leadership positions."

Like other MGH notables, Dr. Potts schedules periodic trips to lecture or take part in scientific meetings. He recently spent 10 days in Russia conferring with Soviet scientists on how extended space flight might affect the bones of spacemen.

He tries, however, to restrict his travels to less than 40 days a year. "While it's important to communicate with others in one's field," he said, "one must not fall into the trap of becoming the TWA Professor of Elsewhere while critical work at home lies undone."

Dr. Potts thus is also able to spend more time with his wife, Susanne; daughter, Martha, 18, a freshman at Yale; son, John, 17, soon to enter

Dr. John T. Potts, Jr., (right) conferring with Dr. Farahe Maloof of the Thyroid Unit

Dr. Alexander Leaf (right) makes a point in a talk with Drs. Cecil H. Coggins and Nina Rubin of the Renal Unit.

Retaining Health Through Proper Living

"We're all going to die of something someday," said Dr. Alexander Leaf, "so the name of the game in medicine is really to keep people active, vigorous, and healthy for as long as possible.

"Hospitals are quite correctly committed to curing those who become sick, but since treatment often becomes technologically complex as well as costly to the patient, the medical profession should focus on additional means of bringing about a potentially enjoyable life."

For years, Dr. Leaf, the Chief of Medical Services at the MGH, has studied cultures worldwide to determine what factors contribute to a maintenance of well-being.

On May 1st, he will be able to pursue that interest in a more direct and formal manner as he steps down from the administrative position he has held at the hospital for 15 years.

Dr. Leaf will become Chairman of a newly organized Department of Preventive Medicine and Clinical Epidemiology at Harvard Medical School and serve as Ridley Watts Professor of Preventive Medicine.

A noted specialist in diseases of the kidneys, he will also become Chief of the MGH Renal Unit which he founded 25 years ago.

Dr. Leaf expects to devote about half of his time to the Renal Unit and the remainder to preventive medicine, particularly efforts to define more clearly and demonstrate what the ingredients are for wellness.

In 1972, under sponsorship of the National Geographic Society, Dr. Leaf visited three remote areas of the world where elderly people were leading full and productive lives. He was anxious to learn whether heredity, diet, exercise, lack of stress, the geographic environment, or a combination of these influences, account for the longevity of the residents. Some claimed to be very old. When proof was possible, however, the elderly, although still of advanced years, turned out to be considerably less aged than they said.

The doctor's visit to villages in the Andean Mountains of Ecuador, the Caucasus of Russia, and the Himalayans along the borders of Afghanistan and China convinced him that disease is not an essential part of the aging process.

Dr. Leaf expects to establish an MGH Center for Health Enhancement and Preventive Medicine. Under his direction, the Center will do research and develop programs promoting personal health by inducing faithful adherence to wholesome living habits.

A Cardiac Rehabilitation Program has been conducted at the MGH and at Harvard University's indoor track over the past 18 months (*MGH News,* December 1979). Patients with heart problems or risk factors for coronary artery disease, such as diabetes or high blood pressure, undergo closely supervised jogging exercises three mornings a week at the track. At the hospital, the patients can pursue a variety of physically rewarding interests such as participation in supervised exercise activities of a less strenuous nature, a Smokers' Quit Group, or a series of dietary sessions entitled, "Healthy Eating for a Healthy Heart."

Dr. Leaf believes that in their already busy curriculum most medical schools overlook nutrition. He intends to remedy that shortcoming at Harvard.

The new Department of Preventive Medicine also will seek to stimulate interest in occupational health care to improve well-being at the work site.

"This subject is so undertaught that it is almost invisible in the curriculum," Dr. Leaf said.

An Occupational Health Clinic which operated at the MGH from 1949 until 1971 reopened last summer to become a part of the new drive against hazards at the workplace (*MGH News,* October 1980).

Dr. Leaf said a major thrust of his department will be to teach medical students how to think statistically. "Instead of taking a particular action just because somebody has said that is what you should do, the student will learn how to form decisions based on the statistical probability of benefiting the patient," he explained.

"In this way, we will also be stimulating studies such as those being conducted at the MGH by a Medical Practices Evaluation Unit to determine if we are providing the most appropriate and cost-effective care for our patients."

The unit, created by Dr. Leaf and operated by Drs. George E. Thibault

(Concluded on Page 8)

Brown; and son, Stephan, 12, a seventh grader.

All have a great interest in music. The parents are officials of the Cecilia Society, one of Boston's prestigious old choral groups, and Mrs. Potts is a chorus member. Martha sings with the Yale Bach Society. John plays the flute, and his younger brother is a violinist and sings with the Youth Pro-Musica Chorus.

Dr. Potts also describes himself as an avid tennis player "with enthusiasm in excess of talent," a heavy reader of contemporary novels, especially mystery stories, and a "chess player of poor repute." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Dr. Leaf Inaugurated Key Improvements

(Concluded from Page 7)

and Albert G. Mulley, has already found that some patients admitted as a precautionary measure to hospital intensive care might do just as well if, after 24 hours, they went to a less expensive, less intensive setting.

The author of more than 200 scientific papers and several books, Dr. Leaf looks forward to resuming direction of the MGH Renal Unit and stepping up his own studies into the physiology of kidney function in health and disease.

Included among a number of major studies in the Renal Unit is a multicenter investigation, directed by Dr. Cecil H. Coggins, into the natural history and treatment of nephrotic syndrome, a kidney disease characterized by massive amounts of fluids, as well as the presence in urine of large amounts of the protein, albumin.

Another program deals with infections of the urinary tract, in particular how they might affect transplanted kidneys. Drs. Leslie Fang and Robert and Nina Rubin are engaged in these studies.

Reflecting on his tenure as Chief of Medical Services, Dr. Leaf described a number of improvements initiated by his department.

One involved the move of the medical wards from the MGH's Bulfinch Building, opened in 1821. In 1977, they closed their doors and the patients moved into newly built, roomy, semiprivate accommodations in the Bigelow Tower of the Gray Building (*MGH News,* June-August 1977).

Dr. Leaf, who played a key role in designing the new floors, said the change catapulted lower-income patients more than a century and one half in terms of a modern treatment site.

Mindful of the advanced age of many Bigelow patients, Dr. Leaf in late 1979 inaugurated a Geriatrics Unit on one of the new floors (*MGH News,* January-February 1980). The purpose of the unit, headed by Dr. Edward W. Campion, was "to provide expertise for the care of the older patients, to detect and investigate any special difficulties they may have, and to bring their needs into the mainstream of medical attention."

Dr. Leaf also takes pride in his department's role with Pediatrics, Psychiatry, Nursing, Social Service and other MGH Services in the establishment in 1968 of the MGH-Bunker Hill Health Center in Boston's Charlestown district, the MGH-Chelsea Unit three years later, and a general reorganization beginning in 1972 of the hospital's Ambulatory Care services.

"At one time, all members of the Department of Medicine were expected to spend at least one-half day a week in the clinics providing free service to the patients," Dr. Leaf said. "The system proved to be far from satisfactory.

"We then organized a group of physicians who were interested in making a major commitment to ambulatory care. With an understanding that they would have to be self-supporting, the doctors formed an organization called Internal Medicine Associates (I.M.A.) and began a practice that has flourished."

In the group are 20 physicians at the MGH and six each at Bunker Hill and Chelsea who provide general medical care. In addition, a total of 22 specialists stand ready to help with problems involving the endocrine glands, diabetes, oncology, lymphomas, and allergies. Other specialties at the MGH also operate units modeled after the I.M.A.

Not only do patients benefit from the high quality care but young doctors going through their residency programs also have an excellent setting in which to expand their knowledge.

The next step is the hospital's new, nine-level Ambulatory Care Center (A.C.C.) which will house most of the facilities now in the Clinics Building. Many years in the planning, the A.C.C. represents the sum of the input of the entire MGH community.

Dr. Leaf said the new structure will achieve a major advance in health care for those not needing hospitalization. ■

The Bigelow Tower medical area, which Dr. Leaf helped to design, offers patients modern, air-conditioned, roomy, semiprivate accommodations.

MGH News

Vol. 40 No. 3 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS April, 1981

Striving to Know Why Some People Learn Slowly

Using Radiology to Treat Patients

(First of two articles)

The two middle-aged men shared both a room in the Baker Building and a diagnosis. Both came to the MGH seeking relief from sharp pains that knifed through their legs whenever they tried to walk. Their condition is called intermittent claudication.

The villain is atherosclerosis, a severe form of hardening of the arteries. A kind of fat called lipids collected on the inner walls of the vessels carrying blood to the lower extremities. Over time, circulation became seriously impeded.

Although the patients endured the same anguish, their treatment differed. When doctors visited the two men a day after their admission, one had just returned from a surgical recovery room. He lay in bed feeling miserable and facing another week in the hospital. The other patient was up and walking about, munching on a snack, and waiting to go home. He felt fine.

Credit for the speedier recovery went to an increasingly popular technique in a rapidly evolving field called "interventional radiology."

An angiogram (an X ray of blood vessels after injection of revealing contrast material) had clearly indicated that only conventional surgery could benefit one of the men. For the other, a "balloon angioplasty" was prescribed.

After administering a local anesthetic, a vascular radiologist introduced into the patient's main leg artery a small tube (catheter) equipped with an inflatable balloon. Guided by a fluoroscope, the doctor moved the catheter to where a blockage had developed. Repeated inflating of the balloon gradually restored a normal channel.

Once the results had been verified angiographically, all that remained was for the physician to remove the catheter, apply a dressing, and return the patient to his room.

The procedure, a mini-operation, solved his problem faster, with less discomfort, and at much less cost than if he had required full-scale surgery and

(Continued on Page 4)

Using a radiologic technique, Dr. Arthur C. Waltman prepares to replace a bypass tube used for bile drainage in an elderly patient who has obstructed ducts.

When a seemingly healthy child is slow to learn, physicians and therapists team with educators to devise a program aimed at helping the patient improve skills while remaining in as normal a setting as possible.

But what about the cause of the child's handicap?

Parents who bring offspring to the MGH Learning Disorders Unit worry about whether the slowness can be ascribed to some undetected physical or emotional disorder, possibly resulting from heredity.

In an effort to lift the cloud that hangs over learning-disabled individuals, Dr. Peter B. Rosenberger, Director of the unit, is working with colleagues to better understand brain mechanisms dealing with language function.

"The latest studies reinforce what my coinvestigators and I have believed for some time about learning disorders," he said, "and that is that, for the most part, they are not the result of defective or malfunctioning brains. They are, instead, the result of distributions of talents that just don't happen to square with what society requires at that time of the person's life."

The study results, reported recently in the scientific journal *Annals of Neurology,* cited a "strong association" between verbal intellectual deficits, i.e. low scores on the verbal portion of standard I.Q. tests, and a variant brain structure.

"If we can point one day to a distinguishing feature of some learning-disabled people and say that that feature

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114
Telephone (617) 726-2206

Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD

Charles A. Sanders, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Ralph H. Cluff, Jr., *Typography*

EDITORIAL:

Wilhelm Roentgen's Fallout

In 1895 a German physicist named Wilhelm Conrad Roentgen discovered X rays and simultaneously founded a new field in medicine. Within a few months hospitals like the MGH were already enjoying the diagnostic tool. And that is the point. Roentgen's discovery burst into the medical world with obvious implications for diagnosis.

Had the discovery gone no further than to explore the causes of disease, the German physicist's place in the medical firmament would nevertheless be assured. One has but to look at the CT scan of today to see how developments originating from the "germ" of Roentgen's X rays have revolutionized diagnosis. In addition the original X ray has spawned buildings full of other devices employing radiation to detect ills. In some instances the modern radiologists also use non-radiation tools like ultrasound.

Now radiology has branched off in another direction. Instead of diagnosing disease, some radiologists are devising a variety of innovative ways to treat illnesses as well. A series of articles starting in this issue is examining some of these new weapons. They range from stopping uncontrolled bleeding to reaming out clogged arteries. To describe this field, radiologists use the term "interventional radiology."

As new as interventional radiology seems, though, it really is not. For many decades radiologists have employed X rays for treating diseases like cancer. That specialty became so important in itself that many hospitals have broken therapeutic radiology into a separate specialty called radiotherapy or radiation medicine. Were Roentgen alive today, he might be bewildered by the scope of the fallout from his original experiments.

Letter to the Editor

Dear Editor:

I have with interest read your editorial (*MGH News,* November 1980) about convincing patients that they should continue to take their antihypertension pills.

A good "trick" is to tell the patient that to stop taking the antihypertensive pills because the blood pressure has "normalized" corresponds to a city council deciding to remove a traffic light at a crossroads because no collisions had occurred there for years.

It is an analogy which the patients understand and accept.

Johs. O. Hagelsten, MD,
A.M.E.
Anaesthetist-in-Chief
Kommunehospitalet
(Municipal Hospital)
Copenhagen 1399, Denmark

CT Brain Scanner May Help Explain Learning Deficits

(Continued from Page 1)

is also seen with a particular brain formation that is not typical, we will have a handle on a lot of things," Dr. Rosenberger declared.

A superficial inspection of the brain, which resembles a shelled walnut, suggests that the two sides, or hemispheres, are exact mirror images. In more than 90 percent of the population, however, they are not.

According to previous studies by Dr. Marjorie J. LeMay of the MGH Radiology Department, in a majority of adults having CT (computed tomography) brain scans for miscellaneous neurological reasons, the brain's parieto-occipital region situated between the top and back of the head is wider on the left side than the right.

The left hemisphere is known to be dominant for language function in virtually all right-handed individuals and most left-handed ones.

In a study of 53 children and young adults chosen from the patient population of the MGH Learning Disorders Unit and the Language Clinic, Dr. Rosenberger and Dr. Daniel B. Hier, now of Michael Reese Hospital in Chicago, found a significant number had *reversal* of the usual asymmetry.

CT brain scans showed that in 22 (42 percent) of the patients the parieto-occipital region was wider on the right than the left.

This contrasts with Dr. LeMay's previous finding of reversed cerebral asymmetry in only 25 of 100 neurological patients having CT scans for other reasons. And the reversed pattern appeared in only 10 (23 percent) of 44 randomly selected individuals afflicted with mental retardation.

At some point in their school careers, all participants in the MGH study had reading skill deficits of at least two grades. Members of the families of 38 of the 53 had a history of reading or

Photographs: Pages 1, 4 (upper), 7, 8, Myron Daniels; p. 5, courtesy of Dr. Christos A. Athanasoulis.

Writing samples: Page 3, courtesy of Dr. Peter B. Rosenberger.

Drawings: Pages 4 (lower), 6, Harriet Greenfield.

speech disorders, or both.

Twenty-two patients in the project were also classified as late talkers. Fourteen first spoke two-word phrases between 36 and 48 months of age. Eight did not combine words until after their fourth birthday.

Criteria for participation in the research included being found free of any major neurological problems. None of the patients had suffered at any time from an illness or injury which might have affected the brain.

In addition to finding an increased incidence of reverse asymmetry in individuals who were late in developing language skills, Dr. Rosenberger said earlier studies by his group turned up the same pattern in two other types of developmental language disorders: dyslexia and autism.

Dyslexia is the failure of an otherwise intelligent person to acquire reading skills at an expected rate (*MGH News,* January 1969). Most people associate dyslexia with writing backwards. Actually, only a minority of dyslectics do so.

"There's nothing special about reading and writing backwards," Dr. Rosenberger declared. "This action is often noticed in perfectly normal children as they learn to read and write."

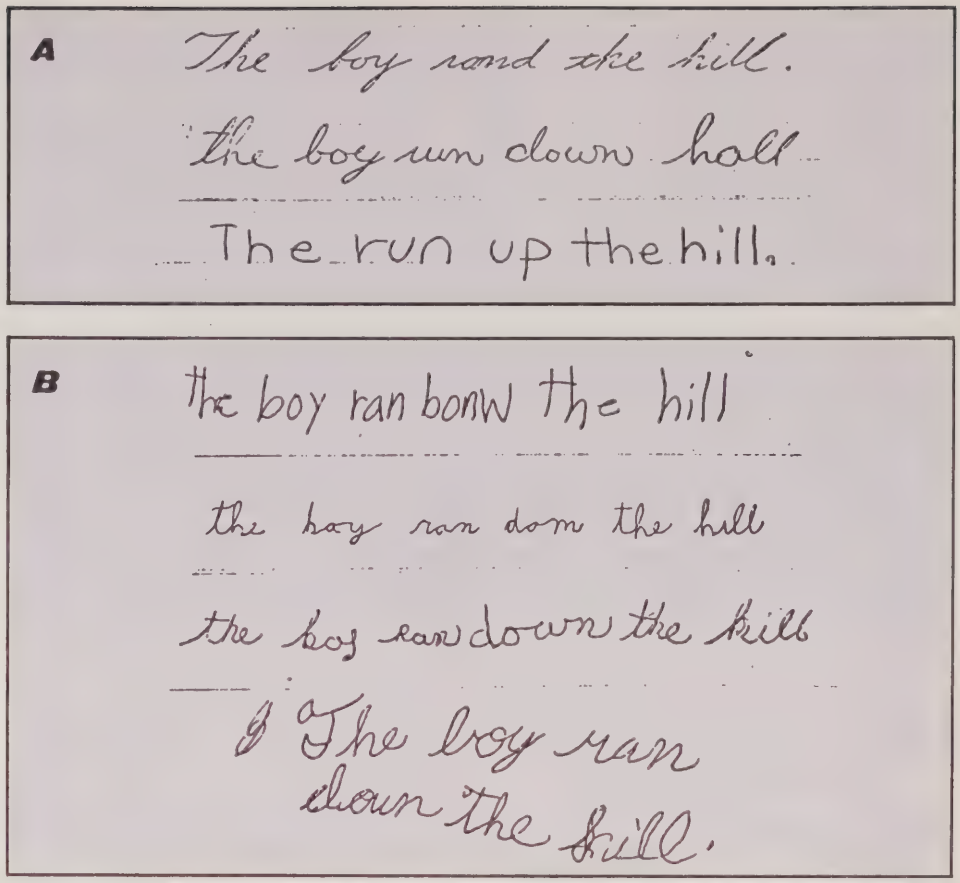
An individual who is autistic not only fails to develop language but also cannot build social or interpersonal skills. He withdraws from society and may engage in peculiar ritualistic behavior.

"In most patients, the condition is essentially lifelong," said Dr. Rosenberger, who is also Assistant Professor of Neurology at Harvard Medical School. "Among those who do develop social skills, the vast majority still are regarded as rather strange and introverted."

Investigating language function in the living brain posed almost insurmountable obstacles until computed tomography, the fastest, safest, and most accurate method of examining the brain's soft tissues, arrived in the early 1970s.

Some researchers first used arteriography (the X raying of blood vessels following injection of contrast material to make them more visible on film), but this procedure can be very discomforting for the patient as well as pose some risk.

With computed tomography, however, the investigators were able to delve into the relationship between functional and structural asymmetries of the brain with a painless and relatively harmless test.


A
The boy rand the hill.
the boy run down hall
The run up the hill.
B
the boy ran bonw the hill
the boy ran dom the hill
the boy ran down the hill
The boy ran down the hill.

Written responses of seven learning-disabled boys to the dictated sentence, "The boy ran down the hill." A verbal or language disability is apparent in the responses of Group A whereas a nonverbal or performance deficit appears to be Group B's problem.

"There is almost surely some significance to the parieto-occipital area being wider on the right than the left in so many of these learning-disabled people," Dr. Rosenberger said, "but we don't know what it is yet because we don't really know what the structures are that we're measuring. Although we can see them on the CT scan, we obviously can't cut into the brain to look further because the people are still alive."

He added that the greatest obstacle to gathering pertinent information in a postmortem is the lack of knowledge of the abilities the patient had. Although compiling a history of the person might seem relatively simple, the details almost always turn out to be inadequate.

Dr. Rosenberger said that he and Dr. LeMay are currently collaborating to solve this problem.

Equipped with a list of 100 patients given CT scans for one of a variety of reasons, Dr. Rosenberger is interviewing every person to inquire about learning abilities in each family. Has learning been a problem for the patient, his parents, brothers, sisters, or any other relatives?

Unaware of the data collected by her neurologist colleague, Dr. LeMay is studying the CT scans for atypical asymmetry patterns. The idea is to see whether the results on the scans provide enough evidence to identify a family history of difficulties in developing skills.

Understanding the mechanisms of learning disabilities and how they may be transmitted can help one day to identify a handicapped child early enough for the acquisition of needed lifelong skills.

At the same time, another interesting possibility arises. If the day comes when a learning disability can be forecast in a youngster on the basis of brain studies and a family history, will it also be possible to predict talent in a young child?

Dr. Rosenberger believes that such a capability is a long jump from where medical investigators stand today.

"We're pathologists essentially," he said. "We've been trained to study deficits, not talent." ■

Dr. Christos A. Athanasoulis (right) discusses a patient's condition with Dr. Robert A. Novelline in the MGH Vascular Radiology Section.

Strict Rules Govern Radiologic Treatment

(Continued from Page 1)

a longer hospital stay.

In addition to widening (dilating) narrowed or blocked blood vessels, radiologists today are equipped in many instances to stop hemorrhages, reduce blood flow in parts of the body being readied for surgery, deliver medicine directly to a site of disease, construct drains to bypass obstructions in ducts, and remove foreign bodies from the blood stream.

Dr. Christos A. Athanasoulis, Chief of Vascular Radiology at the MGH, stressed that interventional radiology is not competing with any other medical discipline. "Our techniques are not always applicable," he said.

Before undertaking any treatment, the radiologists always consult with the patient's primary physician and with surgeons. Together, they decide whether drugs, surgery, or interventional radiology is the most appropriate course.

"The radiologists have developed new ways of handling problems that we have addressed in the past as surgeons, and we consider this a definite step forward," said Dr. William M. Abbott, MGH Chief of Vascular Surgery. "One reason for the success is that the radiologists follow the philosophy that this is a cooperative undertaking."

He explained that very strict criteria govern planning for a patient. If someone suffered, for example, from extensive atherosclerotic disease in an artery, surgical treatment of the entire segment would probably be recommended. But if the patient had a localized problem and no complications, he might be suitable for a radiologic procedure.

Additionally, some people cannot undergo surgery. Inability to tolerate anesthesia is one reason. Another is that owing to a particular set of circumstances the operation would probably not be successful.

In comparison with diagnostic radiology which dates to the turn of the century, interventional radiology is a youngster born only about 20 years ago.

Radiologists in those days had fluoroscopes permitting a continuous X-ray view of a patient, but the specialists had to operate the devices in a darkened room and be satisfied with making a simple diagnosis.

Catheters then available invited little use. Being large and stiff, they posed excessive risk for the patient.

A major advance in X-ray equipment, a so-called image intensifier, brought fast-moving changes. The instrument enabled radiologists to take an X-ray picture from a fluorescent screen, intensify the image, and relay it onto a television screen in a brightly lit room.

The development encouraged modifications in catheters leading to thin, flexible tubes which could penetrate relatively safely and deeply into vessels delivering blood to vital organs of the body.

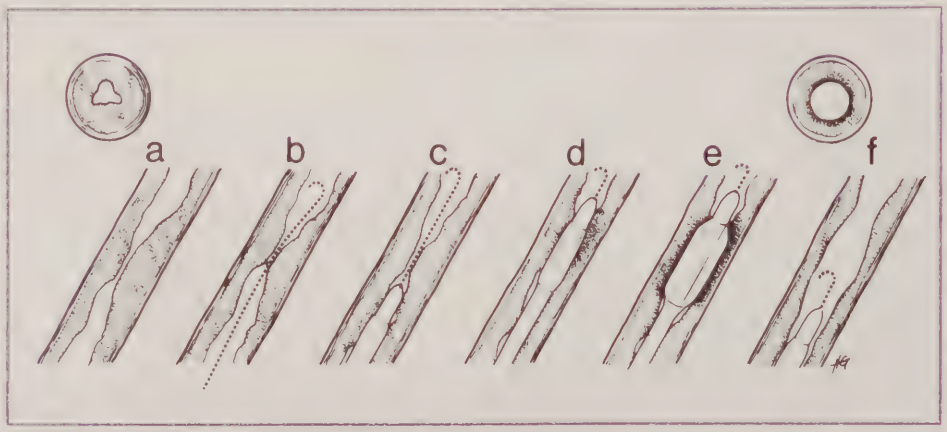
In the early 1960s a typical problem that confronted radiologists was discovering the source of a patient's internal bleeding. Without that information a surgeon found it difficult to operate. The ability to extend a tube through a vessel to an area of bleeding and then send contrast material through the tube to pinpoint on an X ray the site of vessel damage facilitated the planning of operations.

Next, the question arose: Can the bleeding be stopped in some nonsurgical way?

Studies led to a hormone called vasopressin. It stopped the bleeding by constricting the affected vessel. A blood clot (thrombus) could then form at the hemorrhage site.

Response to vasopressin varied, however. In some patients the hormone did not function satisfactorily. Others could not tolerate its infusion because of side effects, i.e. tremors, a "pounding" in the head, cramps, or vomiting.

Someone suggested an alternative. Instead of using a drug, why not try to block the hemorrhage by injecting a



Sketch shows progressive steps for reopening a clogged blood vessel (a) with a balloon-equipped tube introduced into the vessel (b and c). Balloon is inflated (d and e) clearing the passage and then withdrawn (f).

particle of some kind.

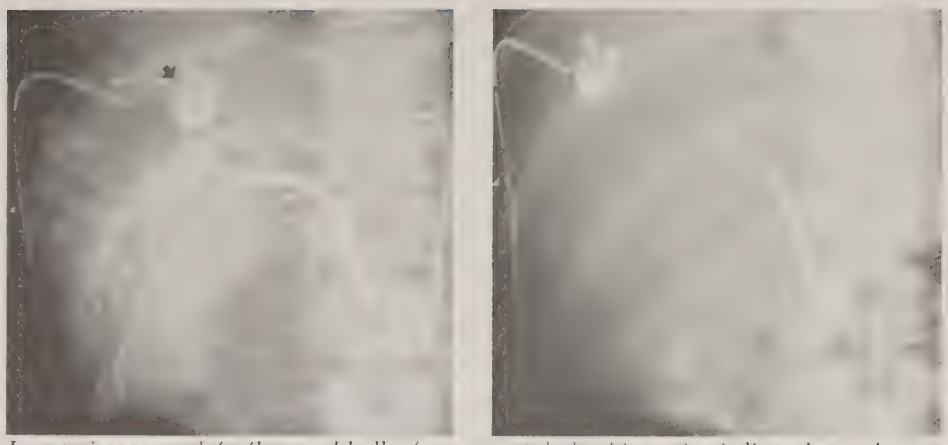
A gelatin called Gelfoam proved to be one answer. To halt bleeding, doctors customarily applied the product to external wounds. By cutting the Gelfoam into tiny bits, the vascular specialists found they could maneuver the pieces through a catheter to the bleeding site in a blood vessel and then plug the ruptured wall.

Embolization, as the procedure was called, caught on quickly after its development around 1970. Soon, physicians extended the technique, originally used to stem bleeding in the GI (gastrointestinal) tract, to other parts of the body.

In 1972, an MGH surgical and radiologic team cited the value of embolization in patients undergoing massive blood loss after suffering pelvic fractures. In an article appearing in the *New England Journal of Medicine,* Dr. Michael N. Margolies, the principal author and a surgeon, described how catheterization and then injection of clotted blood through the tubes controlled hemorrhages in two patients.

In 1979, writing in the *American Journal of Roentgenology,* the MGH angiography team reported that of 20 patients found to be hemorrhaging severely after pelvic fractures, 18 were helped by transcatheter embolization. Before treatment, their blood requirements averaged 32 units. Afterwards, the need averaged only 5 units.

Dr. Athanasoulis, who is also Associate Professor of Radiology at Harvard Medical School, indicated that, in general, control of bleeding is best accomplished by vasopressin in the GI tract and by embolization elsewhere.



In arteriogram at left, flattened bullet (see arrow), lodged in patient's liver, is causing massive bleeding. At right, the bleeding has stopped after sealing of the liver artery break with Gelfoam, injected through a tube.

The past decade has seen "marriages" between angiography and a number of other medical techniques. The coming of age of ultrasound (high pitched sound) and computed tomography (CT scanning), for example, gave radiologists the capability of guiding catheters and needles to just about every area of the body where disease, such as tumors, abscesses, or cysts, might appear.

Using selectively placed catheters, doctors can deliver high concentrations of medicine to disease sites. Similar quantities of drugs, given throughout the body, might lead to adverse side effects.

Radiologists often work with surgeons in the treatment of patients. Suppose a person has an abscess in the liver. Using the various methods available, the radiologist can map the location of the pus-filled pocket and introduce a needle to drain the infection. If this proves unsatisfactory, a surgeon can then proceed to operate, knowing the precise location of the abscess.

Another example of such cooperative effort concerns patients suffering from pulmonary embolism (blockage of a lung artery by a blood clot). Most of the patients receive blood thinners, but people who bleed easily cannot tolerate these drugs. Working as a team, the vascular surgeon and the radiologist will install protective filters in a major vein carrying blood from the legs. The filters are designed to snare or break up any clots before they can reach the lungs.

Unlike direct surgical clipping of the vein which requires an operation with general anesthesia, the radiologic technique is conducted under local anesthesia and puts less strain on the patient.

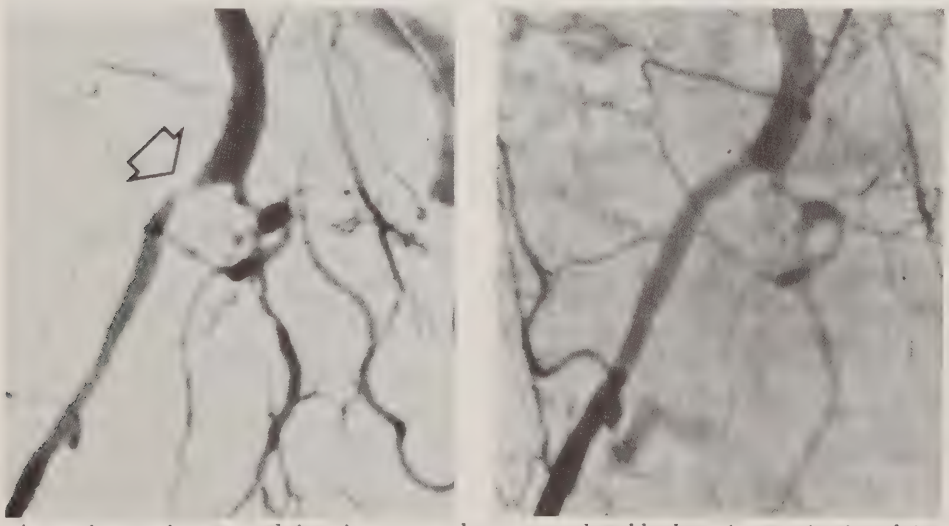
A catheter installed as a bypass is enabling a grandmother to lead a normal life. The woman, close to 70, developed tumors in her liver bile ducts. Because of their location, the tumors could not be operated on, and they blocked the bile from reaching the patient's intestines to aid in digestion.

"In such situations," Dr. Athanasoulis said, "the bile produced in the liver sometimes gets into the blood stream and causes fatal complications."

Through the skin, vascular radiologists ran a tube to the liver and from there to the intestines, in essence permitting the backed-up bile to drain around the obstructions by means of the catheter.

That was four years ago. Every two to three months, the grandmother visits the MGH's Vascular Radiology Section to have the tube replaced, and on every trip she brings a homebaked Italian cake.

(To be continued)



Arrow in arteriogram at left points to an almost complete blockage in a patient's pelvic artery. After use of a balloon catheter, the vessel, seen again at right, has regained a normal blood flow.

Hernia Pain May Be Signal for Surgery

Misconceptions about hernias abound.

Although second on the nation's list of surgical repairs (next to a D and C, or dilatation and curettage, in women), hernias present such a study in contrasts that confusion is understandable.

Most people with hernias live perfectly normal lives. Many do not even know that they have the condition, which may appear at birth or be acquired later. Yet, hernias often restrict a person's activity level. And they can become life-threatening.

Also, although surgeons describe the repair work as technically a major operation, they add that for the vast majority of patients the procedure is simple, straightforward, and safe, with excellent results.

A hernia is a protrusion of some part of the body, such as an organ, out of the compartment or cavity which normally contains the part.

Layers of muscle or other tissue form a protective, outer wall around each cavity. When at any point this wall weakens, a thinner, inside lining may bulge outward at the site, just as an automobile tire's inner tube might press against any defect in the tire's outer wall.

The problem may progress no farther. Or it may rupture the outer lining, allowing the inner one to push through the opening and form a hernial sac.

As portions of an organ, such as the loop of an intestine, move in and out of this sac, the patient might sense the presence of a lump off and on as well as local discomfort. The pain, or its threat, will often stop a sufferer from activities such as playing tennis or lifting heavy objects. Bowel habits also may change.

If the intestine became trapped in the pouch (doctors describe the condition as "incarcerated"), the lump would become persistent and give the patient increasing discomfort. Physical activity would tend to aggravate the hernia, making it enlarge and protrude more.

The main threat to the patient occurs if the hernial sac becomes too crammed, swelling up and choking off the blood supply to the contents. A "strangulated" hernia, evidenced by constant severe pain and tenderness, a fever, and perhaps a high white cell count, demands immediate surgical intervention.

Dr. Andrew L. Warshaw, an MGH surgeon, said that without corrective surgery the tissue may die and become gangrenous. If a section of bowel had been caught, he said, bacteria in it could escape and infect surrounding tissue. The infection would endanger the patient's life.

Groin (inguinal) hernias constitute by far the most common complaint. Each year, half a million American males undergo repair of groin hernias. They occur much more often in males than in females.

Dr. Daniel S. Ellis, a senior physician at the MGH, said patients with groin hernias sometimes fear they have appendicitis or a tumor. A manual examination (palpation) of the sensitive area can often enable the doctor to detect a hernia.

"There is no medication specific for an inguinal hernia," Dr. Ellis said. "The patient, however, should try to avoid constipation which in turn would prevent straining."

Unless there is some reason not to operate, such as an accompanying disease that would increase the risk of surgery, Dr. Ellis advises the patient "to have his inguinal hernia corrected surgically. It won't get better otherwise."

In the past, many patients have worn trusses, devices designed to prevent growth of a hernia, but Dr. Ellis regards them as a nuisance, and Dr. Warshaw sees them as a delaying tactic to avoid needed surgery. Dr. Warshaw also warned that over time their constant rubbing against the hernial area might compromise the tissue that would be used in any repair.

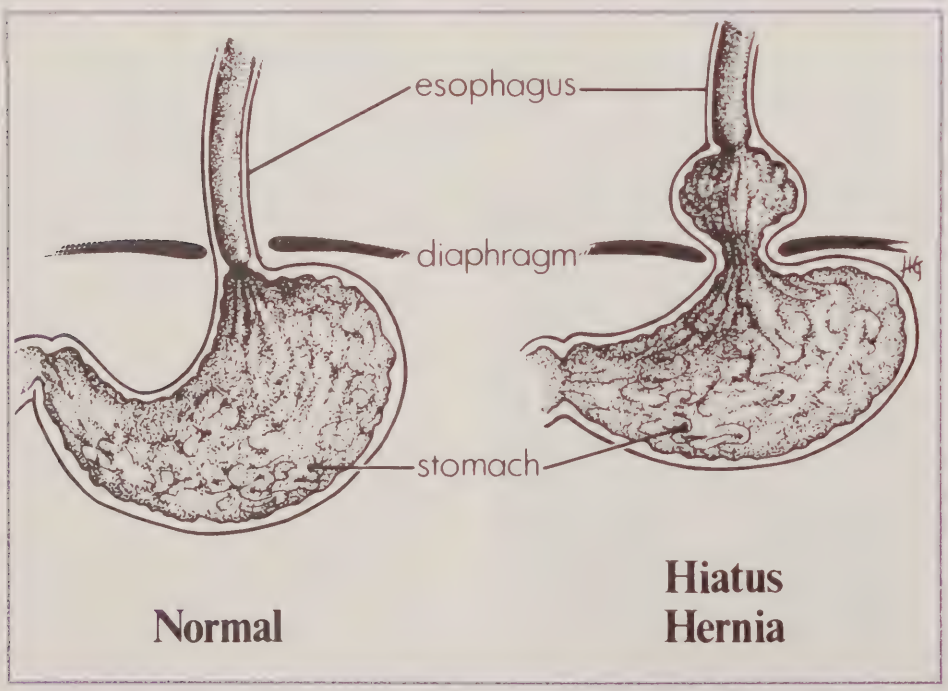
Size alone has little significance in measuring the severity of a hernia. Large ones often present no symptoms or problems. The critical factors are the tightness of the space into which the sac has extended and the degree of compression upon its contents. Thus, the hernia can be small and still pose a serious threat.

Other hernias include:

Femoral—situtated in the thigh, just under the groin, they stem from a weakness in the abdominal lining. In women, childbearing may contribute to the weakness. Surgery is recommended in most instances.

Umbilical—Resembling a bulging navel, these hernias can result from a birth defect or be acquired later in life due to obesity or other strains upon the abdominal wall. In young children, the condition sometimes normalizes without an operation. For those youngsters in whom the affliction persists and for adults, surgery is the only answer.

Hiatus (also called diaphragmatic)—A gap (hiatus) in the diaphragm widens abnormally, allowing part of the stomach to push up into the chest. The vast majority of these hernias require no surgery. The chief symptom is heartburn, produced not by the hernia itself but by stomach acids backing up



A hiatus hernia occurs when the opening, or hiatus, in the diaphragm becomes too wide and allows part of the stomach to slip up the esophagus (food pipe) into the chest.

Improved Methods Of Intensive Care Save More Lives

Barbara Pikl, RN, was one of many members of the Pediatric Intensive Care Unit who fought successfully to save Jimmy Kenny, now 17, after he was struck by a car. Jimmy, shown with his mother, is fully recovered.

Each year in the United States more children between 1 and 14 years of age die from traffic accidents than from drowning, poisoning, and all childhood illnesses combined.

Head injuries constitute the primary cause of death from road accidents, and, despite a declining birth rate, the number of casualties has been increasing.

In the last several years, however, techniques to combat severe assaults on the brain also have multiplied. While health professionals may debate the importance of individual procedures, few doubt that together the treatment methods have made an impact on the recovery potential of victims.

Speaking in March at an MGH medical meeting (Pediatric Grand Rounds), Dr. Mark A. Rockoff, Associate Director of the hospital's Pediatric Intensive Care Unit (ICU), told of an Arlington, Mass., teen-ager who suffered nearly fatal injuries two years ago when struck by an automobile.

Hurled through the air by the impact of the collision, Jimmy Kenny landed on his head. After initial treatment at a community hospital, he was transferred to the MGH. Complications were developing, including a soaring pressure within his head.

"The most feared development in a head injury is brain herniation," Dr. Rockoff said. "That is, if the ICP [intracranial pressure] goes up too high, it can actually cause the brain to shift and become distorted. In Jimmy's situation, the brain moved and was beginning to interfere with his breathing." He had remained unconscious since his accident.

Conventional treatment proved insufficient. The measures included the administration of mannitol and steroids, drugs to minimize brain swelling; use of a respirator with extra oxygen to support breathing, and acceleration of the respirator to help reduce carbon dioxide in the patient's blood. This, in turn, constricts some of the blood vessels in the brain and reduces pressure on it.

Jimmy's condition deteriorated until he could no longer breathe on his own. On an ICP scale on which a reading of less than 15 millimeters of mercury is considered normal, Jimmy's pressure measured 37.

Dr. Rockoff, who is also Instructor in Pediatrics and Anaesthesia at Harvard Medical School, said if Jimmy's ICP had remained high, it is unlikely he would have survived.

His treatment, however, directed by Dr. David Todres, head of the Pediatric ICU, included the use of barbiturates after maximum conventional care had failed.

"After the first dose of barbiturates, Jimmy's ICP came down to 5," Dr. Rockoff told his medical colleagues. "With the barbiturates given in conjunction with standard therapy, the patient's pressure remained well controlled. He regained consciousness, and his chances of recovery improved considerably."

Jimmy went home after about a month in the hospital. Today, at 17, he is a senior in high school, looking ahead to college studies leading to a career in law.

(Concluded on Page 8)

---

into the food pipe (esophagus).

"To control this type of hernia," said Dr. Ellis, an Associate Clinical Professor of Medicine at Harvard Medical School, "the patient should adopt proper eating habits, avoid overloading his stomach, particularly with spicy foods; take antacids when necessary, avoid lying down soon after eating, and sleep with the head of his bed elevated six inches higher than the foot."

Incisional—These hernias occur in areas of previous surgery as a result of some undue strain which has prevented the wound from knitting properly.

"In some situations where the tissue around the hernia is inadequate or has been destroyed, the surgeon will use a type of plastic mesh to provide support," Dr. Warshaw stated.

In examining a patient who has one of the abdominal hernias, Dr. Warshaw, an Associate Professor of Surgery at Harvard Medical School, said he checks on three possible underlying conditions because "the same causes that produce a hernia will also tend to ruin the repair job."

He looks first for signs of a colon cancer that could be responsible for abnormal degrees of constipation. Secondly, are there any urinary tract obstructions, particularly in the prostate area, accompanied by increased strain to pass urine? Third, he examines for any lung disease, such as a chronic cough, which might be putting pressure on the abdomen to drive the diaphragm up.

Some surgeons perform a hernia operation (herniorrhaphy) under local anesthesia. Others prefer using a general anesthetic. Today, some patients can go home only a day after their operation, but they must expect to restrict activities for a few weeks.

Following a successful hernia repair and adequate healing time, patients should be able to return to a completely normal activity schedule.

"The repair," Dr. Warshaw said, "should be good enough to hold under any conditions, whether they involve heavy labor, energetic athletics, or unexpected stress." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Better Ways to Judge Patient's Progress

(Concluded from Page 7)

Several barbiturates can help to reverse elevated intracranial pressure, but some have disadvantages. Methohexital and thiopental are ultra short-acting anesthetic agents, often used in an operating room but not always suitable for long-term benefits in an ICU. Phenobarbital is sometimes considered, but it is very long-acting. It can put a patient to sleep for up to a week. The tendency in the MGH's Pediatric ICU is to employ pentobarbital because it is easiest to control.

"Barbiturates are not always the answer," Dr. Rockoff said. "Certainly there are patients who don't respond to these drugs after they've failed conventional therapy. Those patients usually die. But by and large, barbiturates have added another dimension to what we can do for some patients who are otherwise untreatable."

Sometimes, a child's condition is complicated by the presence of intracranial blood clots (hematomas). Dr. Paul H. Chapman, Chief of Pediatric Neurosurgery, or a colleague will operate. Jimmy, however, had no such difficulties.

In recent years, the treatment of head-injured patients has also been assisted by CT (computed tomography) scans and an ICP-measuring device called a "subdural bolt."

CT can quickly alert a physician to an abnormally high ICP because as the pressure goes up, it causes brain swelling and a shrinking of the brain's fluid-filled ventricles, or chambers. The CT scan would detect these changes early and enable the doctor to begin ICP monitoring.

Neurosurgeons install the subdural bolt in the skull through a small hole, and the bolt sits in an opening created in the dura, the outermost of three membranes which cover the brain. The device measures the ICP in the space just under the dura.

Dr. Todres said in an interview that in treating a head-injured person a physician must guard against a rise in the patient's temperature.

For some years now, doctors have turned to intentional hypothermia, a reduction of body temperature from the normal 98.6°F to 95°F or below (*MGH News,* December 1980). Cooling the body reduces its oxygen and blood flow needs because of a concurrent slowing down of the patient's metabolism. Proponents of the procedure contend this lowers demands on the brain. Dr. Todres said, however, that, as with long-term use of barbiturates, hypothermia can pose risks.

Doctors, nurses, technicians, and others who attended the Pediatric Grand Rounds not only heard the story of Jimmy Kenny but also the experience of David Szekely, now 8, of Weston, Mass.

Just a few weeks before Jimmy's accident, a car struck David, causing not only a head injury but also fractures of the pelvis and thigh bone and rupture of a bowel.

David Szekely, who won a battle for life in the Pediatric Intensive Care Unit after a traffic accident, visits with Patricia Ruggiero, RN, and Dr. David Todres.

Progressive collapse of lung function brought him to the MGH from an outlying hospital. He had also gone into cardiac arrest but was resuscitated. However, the heart stoppage temporarily cut off the oxygen and blood supply to his brain.

David's history was presented to underscore the need for total care of a critically ill patient. Although the youngster's head injury did not represent his most critical problem, Dr. Todres' ICU team, including Drs. Joseph R. Custer and Robert K. Crone, aggressively protected the boy's brain against possible swelling and treated his lung complications. Either condition could have proved fatal.

Meantime, Dr. Samuel H. Kim, a pediatric surgeon, repaired the ruptured bowel, the most critical of the injuries, and Dr. Michael G. Ehrlich, Chief of Pediatric Orthopaedics, corrected the various bone injuries.

During the initial phase of David's two-month hospitalization, much concern existed about his outlook, including whether he would ever walk again, but he made a remarkable recovery.

Dr. Todres, who is also Assistant Professor of Anaesthesia (Pediatrics) at Harvard Medical School, said that every patient in the ICU has a chance. "Even if somebody says a particular child has only a 1-in-100 chance of overcoming a crisis," he declared, "as far as I'm concerned that child could be the one."

Speaking at the Pediatric Grand Rounds, Dr. Donald N. Medearis, Jr., Chief of the MGH Children's Service, deplored the lack of motorists' concern for the safety of children riding in vehicles. Statistics show that the use of seat belts to protect young motor vehicles passengers would cut the death toll among them in crashes by 50 to 90 percent. ■

MGH News

Vol. 40 No. 4 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS May, 1981

Radiologists Assault Drug-Resistant Hypertension

(Second of two articles)

Of more than 34-million Americans with high blood pressure, between one and two million have an underlying condition unresponsive to drug treatment.

Their problem is renovascular hypertension; that is, high blood pressure caused by inability of an artery to feed sufficient blood to a kidney. The inadequate flow induces the kidney to release abnormally high amounts of a substance called renin which, in turn, precipitates the rise in pressure.

Surgeons treat the condition by installing a graft to bypass the cause of the interrupted flow, either an arterial narrowing possibly present since birth or a buildup of fatty deposits (atherosclerosis) clogging the vessel. This bypass surgery carries a mortality rate of up to five percent.

Today, more than 90 percent of patients with renovascular hypertension are considered likely to benefit from a different course of treatment, one which calls for little cutting, requires only brief hospitalization, and involves virtually no mortality risk.

Doctors describe the artery leading to the kidney as well suited for the newer treatment called a "balloon angioplasty" (*MGH News,* April 1981). The technique involves guiding a small tube (catheter) with an inflatable tip through a blood vessel to the site of a blockage and then inflating the balloon tip to open the channel. The renal artery is short and easily accessible to the catheter of the vascular radiologist performing the procedure.

Dr. Eve E. Slater, Chief of the MGH Hypertension Unit and a pioneer in re-

(Continued on Page 4)

A Sore Jaw? It Could Be Emotional

People frequently react in consistent fashion to such emotions as tension, anxiety, frustration, and anger.

As creatures of habit, they bite their nails, gnash or clench their teeth, or chew on such objects as pencils or pipe stems; all of which often present something else to worry about.

The problem carries the fancy, and somewhat awesome, title of Temporomandibular Joint (T.M.J.) syndrome. It refers to any condition disturbing the joint (on each side of the head) where the ball-shaped top of the jawbone (mandible) sits hinged in a hollow recess of a temporal bone of the skull.

Smooth action of the joints depends on their functioning in unison. As the mouth opens and closes, only the mandible moves, operated by several large muscles.

Studies conducted within the last generation have shed important light on the cause of most T.M.J. disorders.

"Only 5 to 10 percent of temporomandibular joint problems are caused by structural changes within the joint," said Dr. Walter C. Guralnick, Chief of Oral and Maxillofacial Surgery at the MGH. "Such changes include ankylosis [fusion] of the joint, usually arising from an injury at an early age, arthritic destruction of the joint, and displacement of cartilage. Severe deformities and tumors of the joint are rarely encountered.

"Most complaints have involved functional impairment, such as restricted motion, facial pain, or noisy joints, the problem usually originating in the muscles that control the lower jaw."

Dr. Guralnick explained that this can result from an improper bite or, as in a significant number of T.M.J. patients, from emotion-induced jaw habits which lead to fatigue and spasm of the jaw muscles.

To seek a reason for T.M.J. pain, a dentist first studies the patient's bite. A bite imbalance (malocclusion) caused by as simple a factor as an insufficiently leveled tooth filling could precipitate such soreness in a joint or muscles that within 48 hours the patient might be convinced he had a terrible earache. The T.M.J. is only about one-quarter

(Continued on Page 2)

Saturated fat in red meat, which Americans consume to excess, is the greatest contributor in the diet to high blood cholesterol levels. Story on page 5.

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114
Telephone (617) 726-2206

Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD

Charles A. Sanders, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Ralph H. Cluff, Jr., *Typography*

EDITORIAL:

A Teaching Hospital Is a, Well, Er . . .

The name "teaching hospital" is fine—as far as it goes. The trouble is it describes only part of the function. Teaching hospitals do teach. Indeed at any given time, the MGH has more students of a variety of types than many colleges. Also implicit in the designation "teaching hospital" is the basic purpose of patient care. At the MGH, caring for patients dominates the fabric. And with the bright young physicians-in-training constantly questioning their seniors comes an improved patient care quality derived from focusing several minds on a single patient's problem. However, the distinctive nature of care in a teaching hospital is lost sight of in the term. That element is better defined by a name gaining in popularity: "tertiary care hospital." Tertiary care denotes the third and most sophisticated level of care, diagnosis, and treatment. If the patient requires care not provided by a neighborhood health center or community hospital, the next step would be referral to a teaching or tertiary care institution.

Even "tertiary care," or the more obvious "referral hospital," ignores an important consideration. Hospitals bearing such names generally flourish from the fruits of research as well. Research attracts the inquisitive doctor who usually works as effectively in diagnosing the baffling disease or devising the new technique to treat the stubborn patient problem. The patient profits by being among the first to benefit from new methods and technologies.

All things considered, no term fully describes the teaching hospital. Even a cumbersome hybrid like "teaching, tertiary-care, research hospital" would overlook the fact that the MGH also serves as a community hospital for those persons living within a few miles of the complex. Should we then describe an institution like the MGH as a teaching, research, tertiary care, community hospital? Oh, well!

* * * * * *

Two elements in that cumbersome hybrid are linked in a new program announced in a page 7 article. In any teaching hospital among the essential student groups taught are house officers (interns and residents who are already physicians). With hectic schedules the order of the day, these residents seldom have time for anything but participating in the caring of patients. Some unusual residents have always managed to superimpose laboratory work onto their routine. Now, however, thanks to the generosity of patients, the hospital's General Surgical Services has made it possible for selected young doctors to carry out research during a "mini-sabbatical" and then return to patient care. A wonderful opportunity for those who earn it. A splendid potential for patients who may one day benefit from the research.

A Sore, Aching Jaw May Simply Reflect Stressful Behavior

(Continued from Page 1)

inch from the ear canal.

An absence of several teeth on one side of the mouth could also easily explain a bite imbalance.

If the bite appears normal and tests fail to disclose any disease process, the dentist will look to the patient's stress habits as a possible cause of the joint discomfort.

"The patient may need counseling more than anything else, and if the dentist feels ill equipped to handle that, he can refer the individual to a specialist in psychological problems," said Dr. Guralnick, who is also Professor and Chairman of the Department of Oral and Maxillofacial Surgery at the Harvard School of Dental Medicine.

Dr. Guralnick decried what he described as questionable practices whereby T.M.J. patients are put through very expensive and very involved diagnostic consultations when the problem is a relatively simple one which could be treated much more easily.

While every patient with a joint complaint needs a thorough examination, not everyone needs a bite analysis calling for multiple visits, or a large number of X rays, the doctor explained.

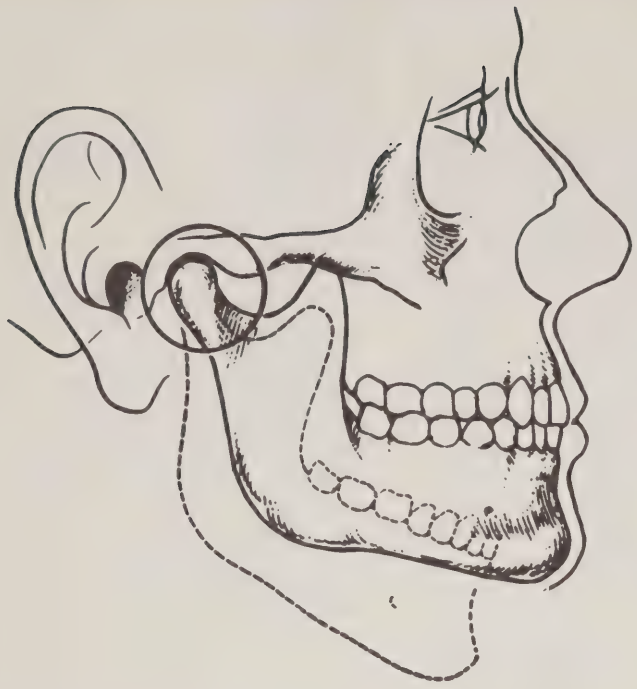
"The treatment resulting from these workups," he said, "very often rests upon a premise that the position of the lower jaw is totally wrong and that the patient must wear an adjustable device over a long period to alter the position of the jaw.

"Along with this come recommendations for speech therapy, biofeedback, and special diets with lots of minerals and vitamins. For the most part, I think this seldom has any bearing on the condition affecting the patient."

Dr. Guralnick told of a woman who came to the MGH recently after being treated for two years by a host of people for what was believed to be T.M.J.

Photographs: Myron Daniels

Drawings: Page 3, Harriet Greenfield; p. 6 (upper), courtesy of MGH Dietary Department.



A bite imbalance caused by as simple a problem as a high filling in a tooth can cause soreness in a jaw joint (see circle in sketch).

difficulties. "We discovered that what she really had was a brain tumor," he said. "She subsequently underwent surgery here."

Within the last 5 or 6 years, advances in X raying joints (arthrography) have sharply increased an awareness of a crippling condition that can occur within the T.M.J.

Just as within a knee joint a cartilage (meniscus) cushions pressure of the thigh bone (femur) upon the leg bone (tibia), so does a meniscus prevent friction between the rounded top (condyle) of the jawbone and its skull socket.

Sometimes the meniscus, which is attached to the condyle, slips out of place and impedes action in the joint. The patient's ability to open his mouth can be severely restricted.

Dr. Guralnick said this displacement also may explain clicking and popping that some people hear in the joint. "A young woman whom I recently sent for an arthrogram had the loudest popping sound you could imagine," he said. "If she were sitting in the next room and opened her mouth, you would hear the noise. The arthrogram showed a markedly displaced meniscus."

To correct the condition, Dr. Guralnick and his colleagues perform a "high condylectomy"; that is, they shave off part of the condyle so that it has more space in which to move in the joint. The meniscus is then put back into proper position.

Of some 300 patients treated at the MGH during the past year for T.M.J. difficulties, Dr. Guralnick estimated that about 25 were operated on for displaced menisci. Often pathologists also reported finding osteoarthritis, a degenerative joint disease, in the condyle as well.

In general, T.M.J. patients seen by dental specialists at the MGH range in age from 30 to 40, and women outnumber men by 6 or 7 to 1.

Of the predominance of females, Dr. Guralnick said, "I think women hesitate less to check into conditions bothering them. Many men just won't take the time."

He added that T.M.J. complications affect many youngsters of high school age. They often experience loud popping sounds from joints which are also painful. "These patients should be very carefully evaluated," the doctor emphasized. "Stress is behind most of their trouble."

The most common symptom of a T.M.J. disorder is pain, often dull and constant, occurring in a single ear. Usually severest in the morning, the pain may radiate to the temple, neck, or jaw. The T.M.J. may feel tender upon touch, and the jaw may swing toward the painful side of the face as the mouth opens. Occasionally, if muscle spasms are involved, the patient may not even be able to open his mouth.

Unaware of the cause of their affliction, many people initially consult the professional they consider most logical to treat them, the ear specialist (otologist) because of ear pain, the bone specialist (orthopedist) for aching bones, or the neurologist because of recurrent headaches.

Ultimately, if all signs point to the T.M.J. as the root of the problem, the patient winds up seeing a dental specialist, usually an oral surgeon.

Because structural changes are behind only a relatively small number of T.M.J. complaints, surgery is most often not the solution, although any dental defects which can contribute to pain must be corrected.

Dr. Guralnick and a colleague, Dr. David A. Keith, conduct a T.M.J. consultation clinic on Thursday mornings in the Department of Oral and Maxillofacial Surgery.

"The patient needs tremendous support," Dr. Guralnick declared. "Once his or her illness is diagnosed as stemming from the jaw muscles, it is important to approach the problem as a psychosomatic one.

"A sympathetic and thorough explanation to the patient of what is happening can be of great help. Counseling will often quickly ease the tension underlying such habits as grinding or clenching teeth."

The dentist may suggest that the patients wear a so-called bite plate at night and during periods of concentration when they might be apt to clench or gnash their teeth. The bite plate is not unlike a mouth guard that an athlete, such as a boxer, might wear in competition. The corrective device, however, is made of firm, not soft, material.

Patients may need medication to help quell pain and relax muscles. Application of heat can also be useful.

To restore jaw muscles to normal function, the dentist may recommend a soft food diet to lessen the burden of chewing and schedule exercises retraining the jaw to move vertically. The disorder, as indicated earlier, can cause the jaw to take a sideward motion.

With the simple measures that have been outlined, Dr. Guralnick estimates that more than 75 percent of persons with T.M.J. symptoms can eventually be cured. ■

Janet Powers, LPN, whose high blood pressure quickly fell to normal after she underwent a balloon angioplasty.

Study of Radiologic Technique to Intensify

(Continued from Page 1)

search on the effects of renin, praised the balloon method, a product of a rapidly emerging field called "interventional radiology":

"Balloon angioplasties appear to be an effective means of treating both severe hypertension and kidney failure caused by blockage of the renal artery. The technique can be used in patients for whom surgery might pose additional undesirable stress.

"Nevertheless, we do not recommend catheter dilatation in all patients since the duration of effectiveness is still unknown. We will soon participate in a multicenter study to compare the advantages of angioplasty versus surgery in a variety of patients."

In acclaiming balloon angioplasties, Dr. Slater told of a young student at the MGH's Shepard-Gill School of Practical Nursing four years ago who discovered she had hypertension when she and fellow students took each other's pressure as part of their training. Lengthy trials of various medications failed to control her problem.

Referred to Dr. Slater, Janet Powers of Norwood, Mass., underwent a series of tests including arteriography, a special X-ray technique to reveal the condition of her blood vessels. The results showed that the artery to her right kidney had been narrowed by a disease called fibrous dysplasia.

A major decision confronted the 21-year-old girl. She could have a surgical bypass graft or undergo a balloon angioplasty, then very new.

Janet opted for the balloon catheter. Her blood pressure began falling as soon as the radiologist widened the artery. Within a day, the pressure was normal, all medications for hypertension were withdrawn, and Janet was up and about.

Today, she works full time as a licensed practical nurse, caring for orthopedic surgical patients in the MGH's Baker Building. The high blood pressure has never returned.

A major advantage of using the balloon catheter to clear a blocked kidney artery is that if the attempt fails, the patient's physician can still summon a surgeon to create a bypass.

Such an advantage does not extend to all medical conditions which might potentially benefit from the balloon system.

In contrast to the more than 90 percent of renovascular hypertensive patients being eligible for the treatment, only about 5 percent of candidates for heart artery bypass surgery would also qualify for a balloon angioplasty.

Dr. Christos A. Athanasoulis, Director of the MGH Vascular Radiology Section, explained that one of the potential complications of the balloon procedure is that small fragments of atherosclerotic material may pass down a vessel and block (embolize) another artery.

"If this happened in a peripheral vessel, such as in the legs, it would not be clinically important," he said. "But in the heart the development could possibly trigger a myocardial infarction [heart attack]."

Although theoretically possible, such an event has not occurred, however, among more than 1,200 patients listed in a coronary angioplasty registry maintained by the National Heart, Lung, and Blood Institute.

Dr. Peter C. Block, Director of the MGH Cardiac Catheterization Laboratory, said the registry was formed so that medical centers where coronary angioplasties are performed, including the MGH, can pool their data and establish firm patient qualifications for the treatment.

The experience to date, he said, indicates that of patients selected for coronary angioplasties more than 60 percent will have successful results. Most of the others go on to a surgical bypass procedure.

As gingerly as specialists move forward with the balloon technique in heart patients, doctors studying its value in treating narrowed arteries in the brain are exercising even greater precautions.

Balloon angioplasties have been performed in the human brain in only a small number of patients. Although results have been impressive, investigators still have to find a way to minimize the chances of an embolism (blood clot) which could cause permanent neurological damage and even death.

Despite the many precautions that radiologists must exercise in treating patients, the new field of interventional radiology has earned accolades in life-saving episodes.

Recently, a 26-year-old Lynn, Mass., resident who underwent a successful kidney transplant at the MGH in February, 1980, returned to the hospital in a very weak condition. Tests showed that he had a bleeding ulcer in his duodenum, the first portion of the small intestine.

Because John MaDan was taking certain drugs designed to prevent rejection of his transplanted kidney, the platelets, or blood-clotting factors, in his blood were very low. Dr. A. Benedict Cosimi, who had performed the transplantation, felt that further surgery would be too risky.

A team from the Vascular Radiology Section placed a catheter into the patient's bleeding gastroduodenal artery and injected through the tube a type of quick-drying "glue" similar in many respects to what is sold in stores.

As soon as the product touched the opening in the artery wall through which blood was escaping, the glue

Cholesterol: Still Embroiled in Controversy

Probably no substance in the American diet has been targeted for greater, more consistent criticism than cholesterol. Still, after more than two decades of study, much remains to be learned about the effects of this fatlike material in humans.

Although solid evidence supports the labeling of excess cholesterol in the blood as a leading risk factor for the development of coronary artery disease, no one can say unequivocally that lowering cholesterol levels to normal will reduce the risk of heart disease.

"A substantial amount of laboratory data as well as anecdotal examples in humans indicate that lowering cholesterol does make a difference, but so far no one has proved it," said Dr. Lee A. Witters, a physician in the MGH Diabetes Unit who has conducted extensive studies on fat metabolism.

Although confident that researchers will eventually prove the hypothesis, Dr. Witters sees a need in the meantime to eliminate a number of uncertainties and misconceptions concerning cholesterol.

First of all, people should understand that cholesterol is not some deadly toxin, but an alcohol which has the same insoluble properties as fat (lipids), and thus is classified in this group.

Every cell in the human body is made in part of cholesterol. The adrenal glands need it to produce cortisone; the ovaries or testes to make sex hormones; and the liver to turn out bile salts, which aid in fat digestion. Cholesterol is also found in myelin, the material which forms a protective sheath around nerve fibers.

The liver manufactures cholesterol, about 1,000 milligrams (.035 ounce) a day. In addition, the average adult American consumes about 600 milligrams of this lipid each day. Cholesterol is found solely in foods from animal sources, such as meat, eggs, butter, and cheese. Plant foods, such as grains, fruit, vegetables, and nuts, are free of cholesterol.

Speaking at an MGH medical meeting (Cardiac Grand Rounds), Dr. Witters said that much confusion exists over what constitutes an abnormally high cholesterol level in the blood. In some laboratories, he said, test results are evaluated statistically; that is, a

(Continued on Page 6)

solidified, forming an instant plug and preventing further bleeding.

The capabilities of interventional radiology are many; dilating an artery, stopping a hemorrhage, delivering medicine to the site of disease, reducing blood flow in an area being readied for surgery, bypassing biliary obstructions in the liver, retrieval of foreign bodies from the blood stream, and the installation of filters in major veins to prevent clots from reaching the lungs.

In the opinion of many physicians, the treatment possibilities created by interventional radiology are just beginning to be realized. This presents a challenge: training sufficient people in radiology to do the job.

"We think we're meeting those responsibilities at the MGH," said Dr. Athanasoulis.

Residents in radiology at the MGH spend three years learning the basic principles of the specialty, and then devote a fourth, sometimes a fifth, year to a subspecialty as a so-called Clinical Fellow. In Vascular Radiology, three such Fellows are presently being trained in all aspects of this field's treatment methods.

Dr. Juan M. Taveras, MGH Chief of Radiology, also has established a Visiting Fellowship program. Radiologists from anywhere in the country can come to the MGH for a week or two to observe and be formally taught in their area of interest, including interventional radiology.

This month, some 200 radiologists from the United States and Canada gathered at Boston's Parker House Hotel for a four-day course on interventional radiology with workshops focusing on methods and materials.

Directed by Drs. Athanasoulis and Arthur C. Waltman, the course was presented under the auspices of Harvard Medical School's Department of Continuing Education.

A new textbook, *Interventional Radiology,* reflecting the "state of the art" as practiced at the MGH, will be published this summer by W. B. Saunders Company of Philadelphia. In addition to Dr. Athanasoulis, the book's editors are Drs. Reginald E. Greene and Richard C. Pfister, both of the MGH, and Dr. Glenn H. Roberson, formerly of the MGH and now Radiologist-in-Chief at Albany Medical Center Hospital in New York.

"Even as we teach others about this area of medicine, we continue to gain additional knowledge ourselves," said Dr. Athanasoulis. "But one thing has been apparent for a long time. Interventional radiology very often means less strain, discomfort, and risk for the patient than surgery. And the patient can sometimes leave the hospital the same day, which means quite a financial saving to him." ■

In the MGH Vascular Radiology Section, Drs. Alan J. Greenfield (left) and Arthur C. Waltman judge whether a radiologic procedure would be appropriate in treating a patient's blood vessel problem.

Cholesterol-conscious dieters avoid most dairy products containing fat.

Vegetarians Avoid Cholesterol Problems

(Continued from Page 5)

team may assay the blood of a thousand people, find the mean cholesterol value, and then, by statistical analysis, determine that everyone in the top five percentile has an abnormal result.

"If you do that for the American population, then we're talking about 280 milligrams percent and up being abnormal," he said.

"Many studies have shown, however, that the risk of clogging coronary arteries with cholesterol begins when its level in the blood climbs above 200 milligrams percent. On this basis, as many as half of the American people have a cholesterol value which falls into the unhealthy range."

In contrast to Americans used to a diet of too much cholesterol-heavy foods, such as red meats and dairy products, the Japanese and Chinese enjoy cholesterol levels averaging only 130 milligrams percent.

Can a population with such values be found in America? Dr. Witters points to vegetarians.

"Many vegetarians eat dairy products as a source of protein," he said, "and often consume excessive quantities of eggs, extremely rich in cholesterol. Yet their cholesterol levels are very low, perhaps 160."

This would seem to incriminate red meats as the major element in the diet hiking blood cholesterol. Dr. Witters described the saturated fat of meat as the main villain.

"Saturated fat causes certain metabolic actions," he said, "which can have an even more potent effect on blood cholesterol than if the patient had consumed the substance in a pure state."

In recent years, much interest has focused on research indicating that not all forms of cholesterol are health-threatening. One type actually seems to protect arteries. It is called a "high-density lipoprotein" (HDL).

Since lipids are insoluble in water and blood plasma consists mainly of water, the lipids must have a method of transport for absorption in tissue. So they team up with protein; thus the name, lipoprotein.

Besides being appetizing and nutritious, fruit is free of cholesterol. Because of a high concentration of fat, however, coconut and avocado should be avoided by persons seeking to lower their serum cholesterol.

Various investigations have produced data suggesting that a "low-density lipoprotein" (LDL) is what is deposited in the walls of arteries and that HDL actually extracts LDL from the vessels. The bottom line seems to be that if the makeup of cholesterol can be manipulated so that LDL is lowered and HDL is increased, a principal risk of coronary artery disease can be eliminated.

"The picture is an intriguing one," said Dr. Witters, who is also Assistant Professor of Medicine at Harvard Medical School, "but the work on these lipoproteins is still in the investigative stage and not ready to be translated into everyday patient-care practice. Many things remain to be sorted out."

For one thing, the doctor remarked, some laboratories are having trouble measuring lipoproteins. He pointed out that even small errors in an assay can translate into big errors in an interpretation of risk.

If one's total cholesterol (the amount present in all of four types of lipoproteins) is below 200, indicating a healthy level, there is no reason to think that a low HDL would have any impact.

"A low HDL would be significant only if total cholesterol measured abnormally high," Dr. Witters said, "because then there would be two components to the patient's risk of developing heart disease."

Many factors can affect the concentration of HDL in the blood. Researchers theorize that ovaries or some female hormone may be reponsible for women having higher HDL levels than men. The fact that fewer women develop heart disease than men would seem to support the theory of HDL protectiveness.

Dr. Witters said that HDL can be increased in a number of ways: physical exercise, loss of excess weight, cessation of smoking, reduction of sugar in the diet.

In the face of encouraging word about the potential of HDL comes research findings of a disquieting note. There are studies which indicate that lowering blood cholesterol could result in a slightly increased incidence of cancer.

Dr. Witters described the evidence as very weak and controversial. The National Heart Institute and National Cancer Institute also agreed that the risk of heart disease from high cholesterol appears to exceed the small and

Surgical Fellowships Widen the Careers of Gifted Doctors

An MGH fellowship awarded to Dr. Craig W. Lillehei will permit him to continue studies in immunology.

In a program believed unique among American teaching hospitals, the MGH is offering special opportunities for career advancement to outstanding members of its surgical house staff.

Dr. W. Gerald Austen, Chief of General Surgical Services, has announced establishment of a fellowship program which each year will enable as many as five young doctors to gain thorough knowledge of a specific scientific area important to surgery.

"We feel, first and foremost, that everyone in the MGH surgical program should be trained to be an outstanding surgeon," Dr. Austen said. "However, a program like ours includes a sizable number of individuals who are also exceptional in terms of scientific interests and innovative thought.

"As a result of gifts made to the hospital over the years by grateful patients, we can help these talented house officers take a year or more to delve into research, learn new techniques, and in general begin that phase of their career in which they hope to perform some really meaningful scientific work."

Creation of the fellowships also permitted the hospital to honor five of its noted surgeons, men who not only built international reputations in their respective fields but also engendered tremendous personal admiration from colleagues in the hospital.

Dr. Austen announced winners of the following fellowships, which begin July 1:

The Marshall K. Bartlett Fellowship in general surgery to Dr. Craig W. Lillehei, enabling him to continue investigations in immunology as a member of the hospital's Transplantation Unit, directed by Dr. Paul S. Russell.

The Edward D. Churchill Fellowship in cardiothoracic surgery to Dr. Ronald G. Tompkins, who is currently studying for a Ph.D. degree in the Department of Chemical Engineering at Massachusetts Institute of Technology. The fellowship will permit him to complete work on the basic mechanisms of atherosclerosis (hardening of the arteries).

The Robert R. Linton Fellowship in vascular surgery to Dr. Richard P. Cambria. He will study with Dr. William H. Abbott, MGH Chief of Vascular Surgery. Dr. Cambria plans studies regarding the physical properties of normal arteries and the development of artificial arterial conduits with physical characteristics to minimize clotting.

The Claude E. Welch Fellowship in general surgery to Dr. Randall D. Gaz, enabling him to work with Dr. Henry M. Kronenberg of the MGH Endocrine Unit. In studies conducted both at the MGH and at M.I.T., they hope to learn how the gene coding for human parathyroid hormone is turned on and off.

The MGH also established the Varaztad H. Kazanjian Fellowship in plastic and reconstructive surgery, but no award was announced for this year. The selections committee emphasized that it will not necessarily award all of the fellowships each year.

Those among the 63 members of the surgical house staff who receive fellowships are guaranteed reacceptance into the regular training program upon

(Concluded on Page 8)

uncertain danger of cancer. The two federal branches, however, ordered investigations to determine whether an association does exist between low cholesterol and cancer, and, if so, just how serious the link is.

At the MGH, Dr. Witters is engaged in studies to try to understand how the body's cells make fat. Last month, he was awarded a John Simon Guggenheim Foundation Fellowship to undertake a year of research in fat metabolism at Dundee University in Scotland. He leaves in July.

As work goes on in many areas—some on the basic cellular level such as that of Dr. Witters, and some aimed directly at improvement in patient care—patients worried about cholesterol ask: What can I do about it now?

Dr. Witters believes that whether concerned about cholesterol or not, everyone should have it checked. At the same time, he cautions that when it comes to cholesterol the saying "you are what you eat" does not always apply.

"There are many people who can consume gobs of saturated fat and still have cholesterol levels which are totally healthy," he said. "The explanation may have to do with genetics, environmental circumstances, age, exercise, sex. We just don't know.

"Similarly, some people will be found to have a high cholesterol level even though they ingest little saturated fat. In each instance, the body is probably overproducing its share. The problem is usually a genetic one."

In the general population, however, the treatment of someone with abnormally high blood cholesterol revolves around a low-fat diet, accompanied by such common sense measures as suitable physical exercise and a halt in smoking.

"Basically, we, as physicians, have to solve a classic risk-benefit equation," Dr. Witters said. "We know high cholesterol presents a risk. We know that in most people proper diet will lower the cholesterol level, but we're not certain that the danger also will ease. Since there is no persuasive evidence that a low-fat diet is harmful in any way, it's worth a try." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Honored Surgeons Set Many Marks

(Concluded from Page 7)

completion of their special work.

The Bartlett Fellowship honors a senior general surgeon who for the past eight years has also been Administrative Director of the MGH operating rooms.

A prolific writer on gastrointestinal surgery, Dr. Bartlett served as president of both the Boston and New England Surgical Societies, as a member of the board of the American Board of Surgery, and as a vice-president of the American College of Surgeons.

The Churchill Fellowship pays tribute to a renowned pioneer in cardiothoracic surgery who served as Chief of the General Surgical Services at the MGH from 1948 until his retirement in 1962. He died in 1972.

Dr. Churchill's contributions to American surgery were extensive, ranging from pioneering work on endocrine diseases to the development of techniques repairing disorders of the heart and lungs.

Dr. Churchill developed a program for graduate training in surgery at the MGH that became a model to emulate. Surgeons who trained under him are spread throughout the world, many heading their own departments.

In establishing the Kazanjian Fellowship, the MGH memorializes one of the great leaders responsible for the stature of plastic surgery as a highly respected and much sought-after surgical specialty.

Dr. Kazanjian, who died in 1974, began his career as a dentist but found himself caring more and more for jaw fractures and other facial injuries. During military service in France in World War I, his unusual ability in prosthetic restoration earned him the title of "Miracle Man of the Western Front."

After the war, Dr. Kazanjian earned a medical degree at Harvard Medical School and continued his highly specialized work at the MGH, retiring in 1941 as head of the hospital's plastic surgical team.

In announcing establishment of the Linton Fellowship, Dr. Austen said the MGH honors a man who in his day was perhaps one of the world's top two or three vascular surgeons.

Chief of the MGH Vascular Unit from 1946 until 1965, Dr. Linton developed many surgical techniques, including widely used procedures for the control of bleeding and blood pressure.

He wrote an outstanding textbook, *The Atlas of Vascular Surgery,* published in 1973, as well as numerous articles for major medical journals. He died in 1979.

Dr. Welch's name rounds out the alphabetical listing of honored surgeons. An internationally known authority on abdominal surgery, Dr. Welch is a past president of the American College of Surgeons, the American Surgical Association, and the Massachusetts Medical Society. He holds the highest honor of the American Medical Association, its Distinguished Service Award.

Dr. Welch's Harvard Medical School lectures and instructions in patient care always ensure a large and enthusiastic attendance. Postgraduate courses he has organized in gastrointestinal surgery and malignant disease have attracted doctors from throughout the nation.

In addition to numerous articles, he has authored several books, including *Surgery of the Stomach and Duodenum,* which has been translated into several languages.

All of the surgeons receiving MGH tributes not only made their mark as physicians and surgeons, but also as educators, serving on the faculty of Harvard Medical School. Dr. Kazanjian was the school's first Professor of Plastic Surgery.

Dr. Austen, who is Edward D. Churchill Professor of Surgery at Harvard, said he knows of no other surgical program in this country that offers an endowed research opportunity of this type. "It is the hope of the Surgical Service," he said, "that what these young doctors do in the future as scientists will affect how they and their colleagues in the medical profession treat future patients." ■

The five MGH surgeons for whom fellowships were named included, from left, Drs. Marshall K. Bartlett and Claude E. Welch.

MGH News

Vol. 40 No. 5 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS June–August, 1981

Surgery Renews Use of Disabled, Arthritic Hands

Meeting Patient Needs From Technology

For the past half century, the United States has served as the technological laboratory of the world. With a few exceptions, this has been particularly true in health care. And with improved capability have come many advances in the treatment of patients.

Unfortunately, over the past 15 years or more the cost of health care in America has risen at an alarming rate, and technology is regarded as a major contributor to that escalation.

In an address at the Institute of Medicine, an arm of the National Academy of Sciences in Washington, D.C., Dr. Charles A. Sanders, MGH General Director, said that in expecting high quality health care the public still believes that "more is better, be it related to technology, facilities, personnel, or expenditure of money."

He added that "more is often expected of technology, particularly in the field of health care, than technology was ever designed to provide."

Since 1977, an MGH Medical Practices Evaluation Unit (M.P.E.U.) has investigated the impact of new technologies on patient care. Do they improve quality of life . . . of medical practice? Can the same improvement in care be realized in some less sophisticated, less costly manner?

For its first three years, the Milbank Memorial Fund of New York underwrote the project. *Now a three-year, $698,000 grant from the John A. Hartford Foundation, Inc., also of New York, is announced.*

The Milbank funding enabled the M.P.E.U. to create an extensive data base describing patients, interventions, and outcomes associated with an 18-bed MGH medical intensive care unit (I.C.U.), part of which serves as a coronary care unit (C.C.U.).

Containing more than 200 variables on nearly 4,000 admissions to the unit, the data base has answered such questions as: What kinds of patients use the 18-bed unit? What diagnosis and treatment constitute intensive care? What are the short-term and long-term outcomes? The answers have helped to set priorities for further inquiries.

The John A. Hartford Foundation funding paves the way for the new avenues of study to define further the

(Continued on Page 2)

The inner workings of the human heart are vividly portrayed by this ceramic model. Story on page 7.

Brenda Vautier has a lot of catching up to do, but no one could be happier or more confident. "I see opportunities now that I never had before," she said.

The 36-year-old East Weymouth, Mass., resident lost 10 years of a professional career as a flutist because rheumatoid arthritis crippled both of her hands.

Stricken in 1969, two years after graduating from the New England Conservatory of Music, Brenda not only had to relinquish concert performances but practice as well. Specialists told her that neither medical treatment nor an operation would enable her to play again.

Determined not to give up, she came to the MGH. Dr. Richard J. Smith, Chief of Hand Surgery in the hospital's Orthopaedic Department, thought surgery was worth a try.

In November 1978, Dr. Smith reconstructed Brenda's right hand, returning to their proper position tendons (connecting tissue to bone) which had dislocated to the sides of her knuckles and to the sides of small joints in the index and little fingers. Ligaments (holding bone to bone) also were reinforced.

In March 1979, the doctor repaired his patient's left hand. Tendons in her left little finger also had moved out of place, pulling that finger into what physicians term a "swan neck" deformity. The repair work included insertion of a small tendon graft from her leg to help rebalance the finger.

Only three weeks after removal of a cast from her little finger, Brenda gave her first concert in a decade. "I'll never forget the program at the Slavic Baptist

(Continued on Page 4)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114
Telephone (617) 726-2206

Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD

Charles A. Sanders, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Ralph H. Cluff, Jr., *Typography*

EDITORIAL:

On Little Cat Feet

For all its bluster, technology sometimes has a subtle way of arriving —much like Carl Sandburg's "Fog." The effect is not calculated. It results from the rapidity with which new science bombards the landscape. Take medicine. Each year hundreds of new tests, treatments, drugs, and the like explode on the health care scene.

In general the effect is very positive. These new technologies make it possible to save lives and improve the quality of life. The real problem is at least two-fold. Among the plethora of new devices, etc., are some that represent little or no improvement over what already exists.

In fact they may also prove to be expensive ways to carry out what can already be done more cheaply, and perhaps with less risk. These "advances" tend to fade away. Then there are those improvements which clearly push forward the state of the art. The nub is, however, that the new whatchamacallit may be exploited in ways other than those that are proven superior.

Let's take a mythical device that makes it possible to detect disease processes in the skull. The new tool so improves the ability to diagnose bone disease in the head that someone decides to try the machine on another "bone," the toenails. The result is a new way of detecting fungus. Immediately the machine becomes a favorite for studying toenails. Fine. But should the device be used for toenails if the far less costly procedure of culturing nail scrapings works as well or even better and without danger to the patient? Trouble is that in the rush to application no one perhaps tried to compare effectiveness, safety, cost, etc.

These are among the kinds of considerations an MGH research program is exploring. In progress since 1977, the study is looking at technology in a variety of ways, determining whether some of the uses of a particular device or an entire unit can be more clearly defined.

As a page 1 article in this issue indicates, the investigation is already inferring guidelines. First the Milbank Memorial Fund and now the John A. Hartford Foundation have supported the long-term study. With the backing of such concerned groups, the unit should continue to suggest ways of refining the application of technology.

MGH Study Helps To Estimate Risks Posed by Illness

(Continued from Page 1)

effectiveness of hospital intensive care practices so that physicians can better tailor patient care to individual needs.

In its first formal professional article, published in the *New England Journal of Medicine,* M.P.E.U. investigators reported that some patients admitted to the I.C.U. might fare just as well even the next day in less expensive, general medical settings.

In discussing potential savings, the team wrote that the hospital bill of someone suspected of having suffered a heart attack, the most common affliction treated in an I.C.U., could be cut anywhere from 6 to 26 percent by early transfer to regular care.

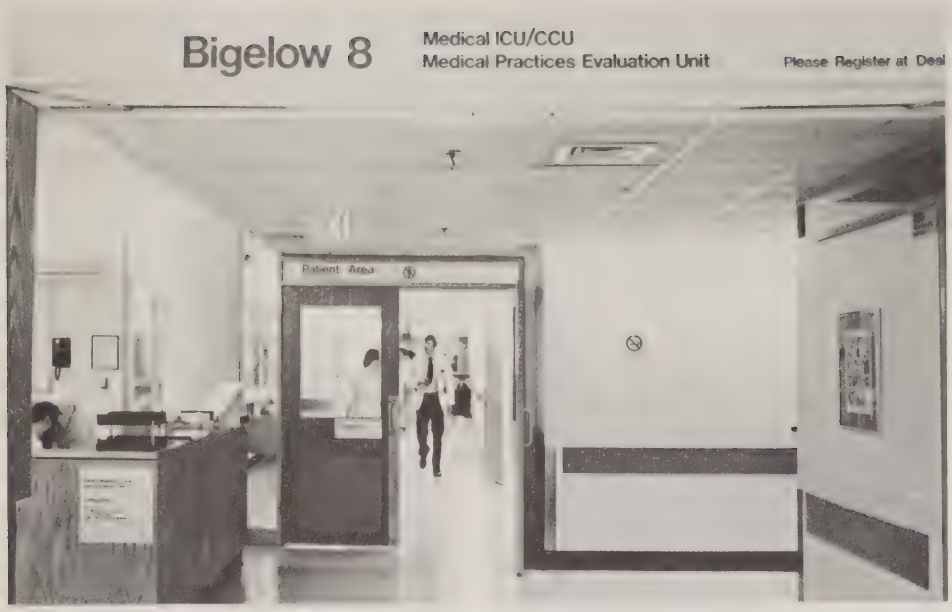
In one of two articles appearing back-to-back in the journal, the probers, who were aided by the hospital's Laboratory of Computer Sciences, wrote that a need for monitoring alone resulted in 77 percent of 2,693 admissions to intensive care during a two-year period.

"Inability to predict which patients would fare poorly without intensive care leads doctors everywhere to routinely assign to I.C.U.s all patients suspected of being critically ill," Dr. George E. Thibault, MGH Assistant Chief of Medicine and M.P.E.U. Director, said in an interview.

Despite concern over possible complications that would make interventions necessary, the study showed that only one in 10 patients admitted for monitoring developed the need for a major intervention. The average hospital bill for patients who, as it turned out, required little or no intensive treatment came to nearly $2,000.

Since many technological advances have been in heart disease, the MGH research included a one-year scrutiny of 360 patients admitted to the I.C.U./C.C.U. with chest pain and indications of having had a heart attack. The results appeared in the second article in

Photographs: Pages 1, 3, 7, Myron Daniels; pp. 4, 5, courtesy of Dr. Richard J. Smith; p. 6 (lower left), from *Venous Problems,* courtesy of Year Book Medical Publishers, and (lower right), courtesy of Dr. Karl A. Lofgren, Mayo Clinic; p. 8, Scott Davis.



Studies of how patients have fared in this 18-bed intensive care unit are helping physicians to evaluate the impact of new technologies on medical treatment.

the *New England Journal.*

The principal author, Dr. Albert G. Mulley, M.P.E.U. Associate Director, wrote that within 24 hours of their admission 168 (47 percent) of the 360 patients were designated as "low risk" on the basis of no major complications as well as acceptable results on tests. These measured the heart's electrical activity and the extent of any heart muscle damage.

The M.P.E.U. team found that low-risk patients had significantly lower rates of eventual diagnosis of a heart attack. Despite shorter intensive care unit stays, after transfer they were also less likely to develop complications that were severe enough to prompt readmission to the I.C.U./C.C.U.

Dr. Thibault, a cardiologist, emphasized in his interview that savings realized by a patient due to early transfer from an I.C.U. are not without a price.

"There is never a point of no risk," he said. "There is a finite percentage of patients who will have some complications after they leave the unit and require readmission. The question is: Will the risk of early transfer be significantly different from the base-line risk that was already there?"

In a recent study, also published in the *New England Journal,* M.P.E.U. investigators reported that in general, with the present state of knowledge, physicians had been unable to clearly identify high-risk patients during their first stay in the C.C.U.

The study showed that 12 percent of patients with confirmed heart attacks who survived their initial C.C.U. stay had to be readmitted—more than half of them within three days of initial discharge—after they developed complications. Twenty-six percent of that return group of twelve percent eventually died in the hospital.

The report whose principal author was Dr. Daniel E. Singer, an MGH Clinical and Research Fellow in Medicine, offered guidelines to single out C.C.U. patients who will likely suffer serious complications of a heart attack.

Recurrent chest pain at least 24 hours after admission to the C.C.U. was described by Dr. Thibault as having the "greatest clinical significance."

Other suggestive symptoms for later complications included: lung fluid sounds called basilar rales, present at admission, especially when accompanied by recurrent chest pain; at least one hospitalization in the previous year, and a history of chronic, obstructive lung disease.

Dr. Thibault said the next step is to study whether longer C.C.U. stays for patients at high risk for recurrence will alter the outcome.

As the work of the M.P.E.U. continues, its members hope to use its data base to answer a variety of questions.

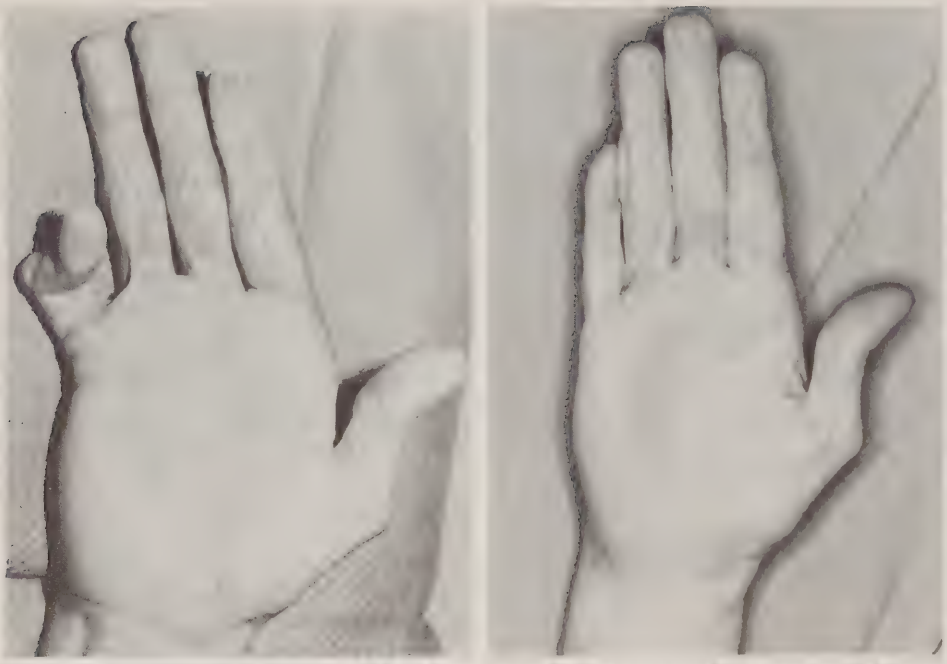
For example, the information being gathered may tell whether individuals treated in a C.C.U. for uncomplicated heart attacks can be discharged safely from the hospital after 7 days instead of the customary 14.

Working with MGH cardiologists and nuclear medicine specialists, the unit also plans to assess the use of a new diagnostic technique, thallium-201 scanning, among patients suspected of having had a heart attack. Can the test speed an assessment of a patient's illness? Is the information reliable enough to permit a reduced hospital stay.

"If physicians could see the future clearly, patient-care decisions would be very easy," said Dr. Thibault, who is also Assistant Professor of Medicine at Harvard Medical School. "We do a lot of things at times because we can't be certain about the future.

"We've got to cover all possibilities to reduce reasonably the risk of serious outcomes for patients. Having better information, such as from the computer data bank we've developed, should enable us to make more accurate predictions, and that, after all, lies at the heart of more effective patient care." ■

Dr. George E. Thibault (left), Director of the Medical Practices Evaluation Unit, and Dr. Albert G. Mulley, Associate Director.



Flutist Brenda Vautier's right hand is shown at left before surgery for severe arthritis and at right following repairs.

Hands Lead Arthritic Repair List

(Continued from Page 1)

Church in New Britain, Connecticut," she declared, "because I played a Handel sonata. I certainly had never thought that I would play classical music again."

Brenda estimates that the operations restored her hands to 90 percent of normal. Her concert schedule includes a program almost every weekend.

Arthritis affects nearly a quarter of the American population, and two arthritics in every five seek medical help (*MGH News,* January–February 1978). Using drugs and other techniques, physicians provide relief for the majority of patients, but many must look further, to the surgeon, for assistance.

Arthritis figures in as many as 100 disorders involving joints and connective tissue throughout the body. Of all the arthritic body parts that are surgically repaired, hands lead the list.

Often in attacking hands, inflammatory rheumatoid arthritis first causes the tissues covering the tendons to swell, making it both difficult and painful to flex and extend the fingers. The tendons may not only dislocate but also rupture.

"Once they fall out of alignment and ligaments also weaken, the joints that are being served become unstable," Dr. Smith said. "The ball and socket of each joint no longer fit properly. At the same time, muscles in the hand may become inflamed and stiff, contributing to a pull of the fingers in one direction or another."

Swollen tissue around tendons in the palm can also exert pressure on nerves to create a feeling of numbness and tingling in the weakened fingers.

In most patients the arthritis is initiated by disease in a synovial membrane which lines both the tendons and joints to provide a lubricant for them.

Although swollen synovium is generally the cause of deformities in rheumatoid arthritis, a wearing away of joints marks osteoarthritis. The erosion, in turn, precipitates inflammation of surrounding tissue.

Two other key types of arthritis can be treated by the hand specialist. A bone broken into the joint or torn ligaments resulting from an accident may lead to posttraumatic arthritis. In some instances, an open wound, such as a laceration, may cause infectious arthritis. The latter has become less frequent because of more rapid diagnosis and improved treatment with antibiotics.

When synovium in rheumatoid arthritis swells out of control, the surgeon may choose to remove the membrane.

"One can do a pretty complete job of removing all the swollen synovium around the tendons," said Dr. Smith, who is also Clinical Professor of Orthopaedic Surgery at Harvard Medical School. "In joints, however, it is often impossible to remove all of the synovium."

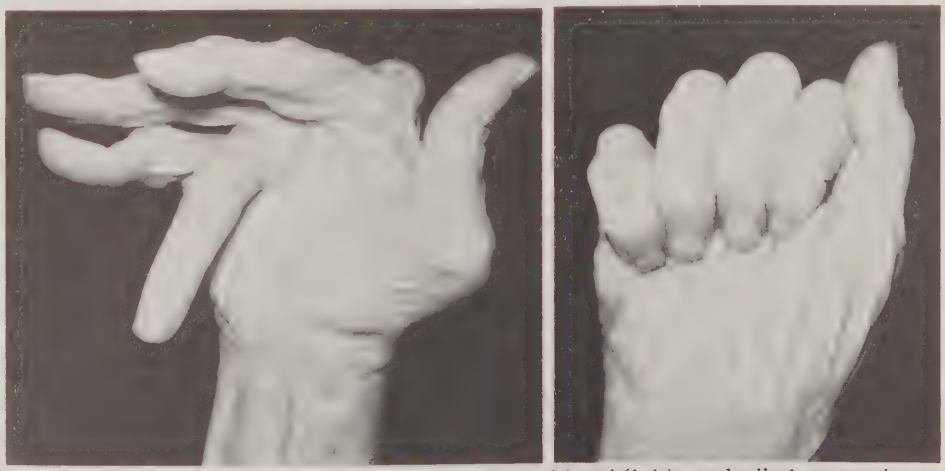
If the patient's condition is mild, medical treatment may be sufficient to control any synovium remaining in the joints. In more serious situations, the surgeon will weigh the risks of extracting the membrane (synovectomy) versus alternative measures, such as replacing the joint with an artificial substitute (prosthesis).

Following removal of diseased synovium, healthy new synovial tissue begins to appear within three weeks.

Dr. Smith said that often when tendons shift out of their normal location, it is possible to reposition them under local anesthesia on an outpatient basis. Under the same conditions, surgeons can relieve pressure on nerves in the hands.

Rupture of tendons requires more extensive work. The surgeon would transfer a tendon from elsewhere in the hand to serve a finger that had been crippled by a rupture. The doctor tells the patient not to expect a 100 percent return to normal, however.

Each finger contains two bending (flexor) tendons. The index and little fingers each have two straightening



Both function and appearance of severely deformed hand (left) markedly improved (right) following implantation of artificial knuckle joints.

Varicose Veins Signal Poor Circulation

The human heart beats 100,000 times a day to pump blood continuously through 60,000 miles of veins and arteries, but the organ does not accomplish the job alone.

Just as a canal employs locks to raise a vessel to a new water level and a mountain railway uses cogs to augment traction, the human body has special methods of manipulating blood flow.

These mechanisms enable the heart's pumping action to cope with the forces of gravity.

After arteries nourish all parts of the body with oxygen-rich blood, veins return the "used" blood to the heart. Dispatched to the lungs to take on new oxygen, the blood is then ready for another cycle.

The returned blood travels from as far as the feet, a long, uphill journey. When the special coping mechanisms function properly, blood flows normally. When they break down, the result is a condition which besets 20-million Americans—varicose veins.

The bulging, bluish lines often visible just under the skin of legs signal the circulatory deficiency.

Varicose veins develop only in the legs' superficial (saphenous) veins. There are two: a long vein extending from the groin to the ankle, and a short one, from the knee to the ankle. These vessels have many branches.

Legs contain two other vein systems: deep veins, which constitute the principal routes for the return of blood to the heart, and communicating vessels, which link the deep and superficial networks.

To combat gravitational pull, the inner walls of veins possess valves which operate like canal gates. As blood travels toward the heart, the valve action prevents reversal of the flow. Deep veins receive an additional pumping assist from contracting muscles in the calves.

Varicose veins indicate something wrong with the one-way valves. Abnormal pressure on the veins may have

(Continued on Page 6)

(extensor) tendons, and the ring and middle fingers each have one. Since a patient's finger can get by with only one tendon of a given type, the surgeon can transfer the second one to replace a ruptured tendon.

Frequently, a surgeon is asked: "Will the brain recognize the new function of a tendon that has been switched?"

"The brain adapts immediately," Dr. Smith said. "Even when many tendons are moved to new positions around the hand, the brain learns their new function almost automatically."

When arthritis has damaged a joint, the surgeon may elect to remove the joint surfaces and then reconstruct the body's own tissues at that site, thus allowing the joint to function again.

In the event a joint is beyond repair, the surgeon has two choices: fusion or a prosthesis.

"The decision depends on which joint is being treated," Dr. Smith said. "With the tip of a finger, the best procedure would probably be to fuse. This would make the finger stronger.

"If the joint is a major one where motion is needed, the surgeon would likely recommend that he replace the joint with an artificial one."

The prostheses come in various forms and may be made of silicone rubber, or metal and plastic.

The silicone products are used more often in the United States.

The rubber implant looks like two golf tees, one standing upside down on the head of the other. After the surgeon drills out the marrow of each bone on opposite sides of the location where the joint was, he then inserts an implant stem into each hole. The broad, middle portion of the prosthesis becomes the new joint.

Dr. Smith said that after one or more artificial joints have been installed, an arthritic hand will usually have significantly less pain, will look better, and will be more functional. However, patients are told not to expect strength and range of motion to become perfectly normal.

While the patient who has undergone a synovectomy is free to do as he likes, and one who has had a tendon transfer regains most of his strength in just a few months, the individual with the prosthesis must exercise care in the use of his treated hand. It will not withstand the stress of heavy labor or forceful athletic exertion.

President-elect of the American Society for Surgery of the Hand, the oldest such organization in the country, Dr. Smith engages in research as well as patient care at the MGH.

"Basically, we're striving for a greater understanding of the mechanisms of the human hand," he said, "so that with restoration of normal balance and stability a patient can regain its many uses."

Meantime, Dr. Smith enjoys hearing from patients he has treated. Brenda Vautier was not the only patient to return to a musical instrument. During the past year, others operated on for rheumatoid arthritis by Dr. Smith and his team went back to the piano . . . the violin . . . and the French horn. ■

Artificial joint implants for fingers come in many forms.

Heredity Plays a Role in Varicose Veins

(Continued from Page 5)

stretched the blood vessels, interfering with the effectiveness of the valves and allowing blood to fall back and form pools (varicosities).

Although principally a cosmetic problem for most individuals affected, varicose veins often induce weariness and a dull ache in the legs, particularly after long periods of standing.

Doctors describe varicose veins as hereditary. Physicians, in fact, would be surprised if in questioning a patient with the condition they did not encounter a familial history of the disorder. However, it is possible, as with epilepsy and many other illnesses, for varicose veins to result from an injury.

Four times as many women as men develop varicose veins. "Female hormones appear to have some special influence on blood vessels," said Dr. Ann B. Barnes of Vincent Memorial Hospital, the gynecological unit of the MGH. "We don't know the specific mechanisms."

Dr. Barnes said that during pregnancy women experience a major increase in their body's production of estrogenic hormones. Consequently, she said, those women with an inherited tendency toward varicose veins may on becoming pregnant develop them at an earlier age than other women.

By resting on veins, the fetus increases the likelihood of varicose veins developing in those women who are susceptible. As the fetus grows larger and heavier, it tends to impede venous circulation. Birth of the child may restore the veins to normal.

From time to time, a varicose vein may become inflamed. Although the condition, called phlebitis, creates pain and soreness, it is temporary. No one knows what brings it on.

In the deep veins, phlebitis may be accompanied by clots (thrombophlebitis), setting off a potentially serious chain of events, including destruction of valves in the vessels, swelling of the extremity, and a formulation of ulcers.

The patient also faces the risk of a clot breaking off from a vein wall and traveling through the blood stream to the lungs. This could prove fatal.

To guard against this, doctors often prescribe anticoagulant medication. For patients unable to tolerate these drugs, a vascular surgeon and a radiologist, working as a team, can insert umbrella-like filters into a vein to snare or dispel any clots before they can reach the lungs.

Unlike the complications that sometimes arise in the deep veins, varicose veins do not pose a lifethreatening situation. The weariness, aches, and unsightly bulges under the skin which the disorder presents usually can be controlled if the patient wears special elastic stockings. They help to prevent dilating of the veins. The stockings are also recommended for uncomplicated, deep-vein problems.

If the patient objects to wearing support hose, and many patients do, surgery can dispose of the varicose veins.

The operation is referred to as vein-stripping. Either saphenous vein can be removed in its entirety without hampering any important bodily function.

The ugly blue welts that one sees on legs are actually situated on branches of the saphenous veins and can be removed individually without extracting the principal vessels. But that could invite a recurrence of the varicosities. Only by removing a main vein would the surgeon render the most complete care.

In some parts of the world, including Europe and Australia, varicose veins are generally not treated surgically. Instead, doctors administer injections to clot the veins, and the patients then wear compression bandages for two or three weeks.

In the United States, specialists regard surgery as more effective and dependable. At the MGH, physicians give injections on occasion for small, troublesome veins and for residual vessels after vein surgery, but the shots are not used as a primary means of treating large varicosities.

The late Dr. Robert R. Linton, Chief of the MGH Vascular Unit from 1946 until 1965, discussed the hospital's early experience with vein injections in his textbook, *The Atlas of Vascular Surgery,* published by W. B. Saunders Co., of Philadelphia.

He wrote that in the year 1840 patients were admitted to the MGH surgical wards for injection of their varicose veins with ferric chloride solution. "The results of this form of therapy were never published," he declared, "and presumably it was abandoned because of serious complications."

He wrote that the use of different hardening (sclerosing) solutions and aseptic techniques commenced again in the 1920s as an ambulatory form of treatment but again was discontinued after a few years because of poor results.

Although varicose veins rank as one of the most common vascular diseases affecting the human race, Dr. Barnes said the number of patients seen with that malady in hospitals is diminishing.

"There are several reasons for this," she said. "For one thing, women, increasingly susceptible during preg-

Patient with varicose veins (left) underwent complete vein-stripping surgery. The legs, shown at right 15 years later, have not had any further treatment.

Restudy of the Heart Offers Some Clues To Sudden Death

Dr. John T. Fallon (left) of the MGH Pathology Department discusses features of the heart with Drs. George Murphy and Rebecca Osgood, also of Pathology.

A dozen years ago as many as one of every five sudden deaths brought to the attention of medical examiners defied explanation.

Today, because of a back-to-basics approach in medicine to learn more about how the human body operates, medical examiners record less than 1 in 10 sudden deaths as unexplainable.

Restudy of the heart's basic structure has permitted much of the diagnostic improvement. The work has led to an appreciation of subtle variances of the organ's anatomy which heretofore had not been very well described, if at all.

Studies indicate that among victims of sudden death in which injury or foul play is not a factor the cause 9 times out of 10 in adults turns out to be a cardiac abnormality, usually coronary artery disease.

Few researchers have looked at the incidence of heart involvement in the sudden death of children, but the pediatric population is coming under increased scrutiny. Early discovery of abnormalities of the heart might later save many lives.

The most common heart condition causing sudden death in children is believed to be a narrowing of the channel through which blood flows from the heart's main pumping chamber, the left ventricle, to the body's main artery, the aorta. Doctors refer to the problem as aortic stenosis.

"The condition takes several forms which together account for probably a quarter of all previously unexplained sudden deaths in youngsters," said Dr. Richard R. Liberthson, an MGH pediatric and adult cardiologist.

Dr. Liberthson told an MGH medical meeting (Children's Service Grand Rounds):

"The person with this affliction may be totally unaware of it prior to a spontaneous, fatal attack. Typically, it occurs in conjunction with strenuous physical exertion."

Dr. Liberthson described the most common type of aortic stenosis as being secondary to an abnormality in which the aortic valve has two rather than three leaflets. In some, the opening between these leaflets may fail to grow as the child grows. Therefore, sufficient blood to satisfy the demands of the growing patient, particularly during exertion, is unable to flow through the valve.

In other patients, aortic stenosis may be secondary to enlargement of the heart muscle beneath the aortic valve. The cause for the abnormal muscle enlargement is unknown. This entity bears the label, "idiopathic, hypertrophic, subaortic stenosis," or I.H.S.S.

Dr. Liberthson said physicians can easily miss detecting I.H.S.S. but that the condition can be identified through a technique called a Valsalva maneuver (named after an Italian anatomist).

While listening to the patient's heart with a stethoscope, the examining physician presses with a hand on the patient's stomach. At the same time, the patient assists by pushing his stomach outward against the hand. If an I.H.S.S. is present, after a few seconds the dual action will enable the doctor to hear a heart murmur of increasing intensity. Often, additional family members may also have I.H.S.S.; thus, screening of relatives is indicated.

Until recently, an I.H.S.S. easily escaped notice during autopsies because the practice of medical examiners or pathologists was to open the heart lengthwise.

Dr. Alan L. Schiller, Chief of the MGH Autopsy Service and Bone Laboratory, said that today if any suspicion of an I.H.S.S. exists, the heart should be cross-sectioned. "In this way, we can better appreciate the diameter of the heart's components," he said, "and any bulge of muscle would be quickly spotted."

The next most common cause for sudden death in young patients is cardiomyopathy, meaning heart muscle abnormality. In some of these patients the heart muscle is abnormally thickened, and in some the heart is dilated. For most of these conditions there is no known cause although some are thought to be secondary to a viral infection. Patients with cardiomyopathy may notice increasing shortness of breath, particularly with exertion.

(Concluded on Page 8)

---

nancy, are having smaller families. That is true at all economic levels. In addition, the national emphasis on stepped-up activity to maintain or improve physical fitness is definitely having a positive influence."

The person with "get up and go" is less likely to contract objectionable varicose veins than the sedentary soul or the one who stands stationary for hours at a time.

Although exercise, such as walking, jogging, bicycling, or swimming, offers no guarantees, any activity that tends to stimulate blood circulation is bound to be helpful. ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114
Address Correction Requested

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Many Problems Can Beset the Heart

(Concluded from Page 7)

Inflammation of the heart muscle (myocarditis) used to be one of the leading causes of sudden death in the young, but postmortem studies conducted in recent years in Miami indicate myocarditis is much less common than before.

"The typical illness in this category was rheumatic fever," Dr. Liberthson said, "but we certainly don't see much of that anymore. Today we encounter mainly viral-caused forms of myocarditis. Some of the viruses are identifiable."

Abnormal formation or location of the coronary arteries may also cause sudden death. Sometimes an artery may not arise from the aorta but from the lung (pulmonary) artery. In other patients a coronary artery may have an abnormal course after leaving the aorta. In the latter group, coronary artery blood flow to the heart muscle may be compromised. These patients may have chest pain or fainting with exertion. Identification of these abnormalities is important because coronary artery bypass surgery can be lifesaving.

In adults, sudden death often results from buildup of fatty deposits (atherosclerosis) affecting the coronary arteries of the heart. In children, this condition is a very rare cause of sudden death and, when present, is inherited.

Children born with a condition called heart block have an increased risk of dying suddenly. A structure called a sinus node, situated in one of the upper chambers (atria) of the heart, normally instructs the ventricles at what rate to pump. If something blocks the signal, like static breaking up a radio transmission, the ventricles develop their own beat, but it is slow. When the rate is very slow, the risk of sudden death is increased. Once detected, this problem can be solved by installing a heart pacemaker.

The list of potential cardiac causes of sudden death runs long, but Dr. Liberthson, who is also Assistant Professor of Pediatrics at Harvard Medical School, declared:

"A careful physical examination, accompanied by appropriate tests and a family history, usually will reveal the problem, however rare."

Referring especially to members of families which include individuals at high risk for a heart attack, the doctor stressed the value of knowing C.P.R. (cardiopulmonary resuscitation) techniques. Use of C.P.R. to continue blood flow to the brain and heart of a stricken patient, he said, would minimize damage while a rescue team, equipped for more definitive treatment, rushed to the scene.

Dr. Schiller, an Associate Professor of Pathology at Harvard Medical School said that in the past if a person died almost immediately after a heart attack, physicians performing an autopsy could not verify that a heart attack had occurred.

Cardiopulmonary resuscitation, being demonstrated here, has saved the lives of countless heart attack victims.

"After a person dies, cells in the body may remain metabolically active for a time," he said. "Until a few years ago, one could not discriminate immediately between live and dead tissue. Before the pathologist could recognize acute dead tissue, there had to be some inflammatory response, and this took time."

Today, heart attacks can be detected very early at postmortem.

The MGH employs what is called a tetrazolium dye to test cells. Dr. John T. Fallon, MGH Director of Cardiovascular Pathology and Chief of Pathology at the affiliated Shriners Burns Institute, explained how the test works:

"We stain cells with this clear liquid, and if the cells are alive, their enzymes pick up the stain, turning it blue. If the cells had died, the enzymes would have been released; consequently the dye would not be picked up."

Dr. Fallon said other types of dyes are used to help evaluate coronary arteries after death. "By injecting dyes of different colors into the arteries," he said, "we can witness the mix and determine which vessels are more blocked than others."

These tests are conducted in addition to more conventional radiologic studies when blood flow abnormalities are suspected.

Dr. Schiller said the days when one individual tries to bridge all the fields of pathology are over:

"We've learned that the team approach is the way to go. Staff personnel in the MGH Pathology Department, for example, are both general pathologists and subspecialists, each capable of offering a special expertise at the autopsy table.

"In the future, we're confident that fewer and fewer death certificates will be marked, 'Cause Undetermined.' " ■

MGH News

Vol. 40 No. 6 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS September, 1981

He Braved the Shoals and Left a Stronger MGH

More Women Drink, Then Look for Help

Inflationary pressures fanning constant changes in America's economic climate have given the nation's labor force a new look.

Today, almost as many women as men pick up paychecks. Government figures show that virtually six out of every 10 households consisting of two or more adults rely on two incomes.

The influx of increasing numbers of women into the workplace, however, is building pressures of an unexpected kind.

"As more women enter the work force and many of them have more disposable income, we find the number of women seeking help at alcohol treatment centers also rising," said Eleanor Z. Hanna, Ph.D., Director of the Alcohol Clinic at the MGH. "The cocktail party is replacing the tea party for many women. The so-called two-martini lunch is no myth."

Much of the concern over stepped-up drinking among women centers on the fact that they often try to match the drinking habits of male colleagues.

"There is a total naiveté among many female patients who come to our clinic about their physiologic inability to tolerate as much alcohol as a man," Dr. Hanna said.

Alcohol dilutes in blood and other body fluids. Being larger in build than the average woman, the average man can therefore absorb more alcohol into his system before drinking affects him.

Additionally, men maintain a fairly consistent level of tolerance for alcohol while in women the level can be quite variable. Menstrual cycles and the use of oral contraceptives, for example, can affect the metabolism of alcohol in women.

The trouble with women problem drinkers is not the number of drinks per occasion but the frequency of the occasions.

On July 7th, Dr. Hanna addressed the national conference of the Canadian Addictions Foundation in St. John's, Newfoundland. She described the latest findings of an ongoing, three-year-old study of drinking patterns in American society.

"Our study revealed that in terms of consumption the woman problem drinker usually does not outpace her normal drinking, female counterpart per

(Continued on Page 2)

Exactly nine years ago Charles Addison Sanders, M.D., became the MGH's 17th General Director with this vow:

"I do not plan to let this hospital languish on its past glories."

Francis H. Burr, Chairman of the Search Committee seeking a successor, reflected on Dr. Sanders' tenure.

"He kept his promise well," Mr. Burr said. "So well that he has carved out a monumental task for the Search Committee."

The task is to find someone as skilled as Dr. Sanders in steering the MGH past the shoals of governmental regulations that are exacting a toll from America's hospitals—particularly the best hospitals. At a time when some institutions have shown signs of slipping, Dr. Sanders left the MGH stronger than when he first grasped its helm.

"The MGH under Dr. Sanders is

(Continued on Page 4)

Dr. Martin Assumes Interim Control of Helm

To keep the MGH on course for the next few months, the Board of Trustees has named Dr. Joseph B. Martin as Interim General Director.

Dr. Martin is Chief of the MGH Neurology Service and is renowned for his study of neuroendocrinology and brain peptides (*MGH News,* September 1978). In addition he is Bullard Professor of Neurology at Harvard Medical School. He came to the MGH in 1978 from Montreal where one of the key positions he held was Neurol-

(Continued on Page 5)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114
Telephone (617) 726-2206

Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD

Charles A. Sanders, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Ralph H. Cluff, Jr., *Typography*

EDITORIAL:

And Regulations . . . And Regulations

Dr. Charles A. Sanders became General Director of the MGH at a perilous time. Once the object of adulation, physicians as a group were beginning to become anathemas to some. Instead of news media praise for the latest "medical miracle," hospitals were incurring wrath for the high cost of those miracles. Reversing hospital costs was impossible. Employee salaries representing by far the largest segment of those costs had in recent years soared. The general rate of American inflation was skyrocketing and carrying hospital costs irresolutely higher. Medicare and Medicaid were peaking in their effect on hospital costs. Malpractice awards were growing nationally. Medical technology was exploding, and the same public which was complaining about medical bills was demanding the latest, most expensive treatment.

Then there were government regulations. And regulations. And regulations. While administrators were still trying to understand the last edict, somebody in Washington or the state capital was busy filing the next. In New York, hospitals figured out that no less than 164 government agencies regulated them. Administrators who should have been planning the future course of their hospitals spent stretches of time completing mounds of government-mandated forms. In addition to wasted time, these regulations packed a one-two punch. First, they cost money, sometimes hundreds of thousands of dollars in order to comply. Second, they tied a Gordian knot around the arms of the administrator. He not only had less time to plan but he also found that new government regulations either prevented or unconscionably and expensively delayed the implementation of those plans. The page 1 article about Dr. Sanders hints at the problems involving the MGH Ambulatory Care Center.

Now under the guise of cutting costs, the Massachusetts Rate Setting Commission is squeezing hospital budgets even more. As the vises of various regulators tighten, medical care is beginning to show some of the results. At least one Massachusetts community hospital has closed its doors.

In some institutions quality of care is starting to look a little frayed. How well the government efforts will control costs remains in doubt. But in the next decade the quality of care in states like Massachusetts will continue to deteriorate. Politicians will ignore a warning like this—until they themselves become the beneficiary of the second-rate care they caused.

* * * * *

This issue of the *MGH News* then is dedicated to Dr. Sanders, the man who refused to let such problems frustrate him; the man who kept the MGH in its position as what some call the world's best teaching hospital.

Women Seek Air Of Sophistication From Drinking

(Continued from Page 1)

event," Dr. Hanna said in an interview. "Regardless of the occasion, the problem drinker will average only two glasses of spirits.

"What sets the patient apart from the normal drinker is that the patient may have established a habit of many more drinking events."

Male problem drinkers will consume 3½ times as much alcohol at each occasion as their normal counterparts.

Women who drink heavily plan these episodes with the expectation of matching the amount of alcohol consumed by their companions and drink between noon and 6 p.m., which parallels drinking times for clinic men.

Studies by other investigators indicate that women tend to drink in response to social pressures and to appear sophisticated whereas men look upon drinking as a means of escaping or finding relief from something.

Of the women patients Dr. Hanna studied, nearly three-quarters had jobs. This compared with a 50 percent employment rate among the normal drinking women.

Increased use of alcohol seemed to correlate with a rise in educational levels. Women from very high as well as very low social standings were more represented in the clinic group than in the sample of normal drinkers.

Data for the study were drawn from interviews with 63 MGH Alcohol Clinic patients and 45 normal drinkers from the Metropolitan Boston area. Participants were asked about drinking episodes experienced over a one-month period.

The participants answered questionnaires posing such queries as: When and where did you drink? With whom? What kinds of drinks did you have (beer, wine, liquor)? Did your companions drink too? How many drinks did you have? Was this more or less

Photographs: Pages 1, 3, 4 (upper), 6, 7 (upper), 8, Myron Daniels; pp. 4 (lower), 5 (upper), MGH Photo Lab; p. 5 (lower), Chris Maynard. *Drawing:* Page 7 (lower), Grace von Drasek Ascher.

Dr. Eleanor Hanna (right) with some members of her Alcohol Clinic staff

than you planned? Was it more than the others had? Did you have food with your drinks? Did you feel under pressure to drink?

A detailed study of each reported drinking event and the behavior of the individuals involved enabled Dr. Hanna's group to determine that among problem drinkers: a "light" drinker had up to 7 drinking events per week; "moderate," up to 19, and "heavy," 20 or more.

Comparable subgroups were formed among the normal drinkers with 2 to 3 events per week placing one in the "light" drinker group, 4 to 7 in the "moderate" group, and 8 to 11, or more, in the "heavy" drinker group.

Why would a light drinker seek professional help? Dr. Hanna explained that while the patient may not yet have developed a physiological dependence on alcohol, either the individual or family members may have begun to sense a psychological dependence.

Also, relatives may urge a woman to seek help after noticing that her drinking routine had become different from that of others in her social group.

Dr. Hanna found that among her clinic patients women who drank lightly tended to drink at home in periods of a half an hour or less, and often in the company of relatives.

The heavier the alcoholic consumption, the wider the range of settings. The individual might never drink at home again but join fellow workers and strangers at restaurants or bars and even drink alone at some out-of-the-way spot, perhaps a park.

The failure of most women to realize that their tolerance for alcohol is much less than that of men poses a serious health danger.

For example, a woman can begin to suffer a degeneration (cirrhosis) of the liver on only a third as much alcohol as a man consumes. The start of the disease in a woman would also be more rapid.

Studies also have shown that pregnant women who drink heavily are twice as likely as lesser drinkers to give birth to babies afflicted with "fetal alcohol syndrome."

This is a condition which in the United States each year affects an estimated 10,000 live births. The children suffer a pattern of birth defects which includes deficiencies in growth and development.

Heavy drinkers, men and women, may face damage to heart muscles as well as a clogging of arteries. Large quantities of alcohol can hamper the body's immune responses, increasing the possibility of bacterial infections. Alcohol may also play a role in the growth of certain cancers caused by other factors.

Dr. Hanna, an Instructor in Psychology at Harvard Medical School, believes it is possible for anyone to become an alcoholic. "Exposure to situations where drinking is not only condoned but also encouraged invites development of a drinking habit," she pointed out. "Often, by simply reshaping one's social environment, a person can avoid the threat that excessive alcohol consumption presents."

Those who exhibit signs of physiological dependence comprise a very small percentage of problem drinkers. The remainder offer a great diversity of reasons for turning to the bottle. Treatment must be tailored to the individual.

It is essential first to separate the problem drinker from the normal one. This can be a difficult task for care givers because often they will be looking at people with very similar drinking patterns who nevertheless exist in different environments or are subject to different internal stresses.

Consider Janet M., in her mid-20s, single, unemployed, and living alone. She very rarely goes to bars but will drink in most other social settings. The longer the event, the more alcohol she will consume. Her friends and relatives also drink regularly.

Although she may be headed toward a drinking problem because she regularly meets the situational demands of a heavy drinking environment, Janet thus far acts normally. She remains well in control of her drinking which is purely social with friends and family.

On the other hand, Margaret P., also in her 20s, presents a different picture. Although her drinking, mainly with friends, does not exceed that of Janet, Margaret is concerned that she may have a drinking problem. She lost two men in her life, one through divorce, the other through illness. Both drank heavily. Margaret's parents are straitlaced. They neither drink nor approve of others doing so.

Margaret's concern may have been generated not only by her two significant losses but also by a need to resolve the conflict between her parents' values and those held by herself and her current circle of friends.

In the 1950s, the ratio of problem drinkers treated in the MGH Alcohol Clinic was eight males for every female. Today the men lead by only three to one.

Since drinking patterns of both sexes are becoming increasingly similar and environmental factors are major shapers of alcohol abuse, Dr. Hanna said it may just be a matter of time before the women drinkers catch up to the men. ■

Outpatient Care Plan Won Top Priority Under Sanders

Associate General Director Lawrence E. Martin (left) and Dr. Charles A. Sanders, General Director for nine years, discuss Ambulatory Care Center (background right). Mr. Martin masterminded the day-to-day construction.

(Continued from Page 1)

clearly one of the world's great hospitals," said Massachusetts Governor Edward J. King.

Some of the evidence of change under Dr. Sanders is physical. For 26 years the institution had struggled to build a new outpatient building.

"The present one is a relic, an extremely difficult place in which to deliver warm and efficient care," said Dr. F. Sargent Cheever, Chairman of the Board of Trustees. "Cramped rooms permitting little modern equipment were just part of the problem. Elderly patients having to trudge from building to building through the winter snow was another."

In the next few weeks the hospital will begin to phase in the occupancy of the new structure. A little later, patients will receive total outpatient care without having to leave the brick and glass walls. Examinations, X rays, day surgery, and a satellite pharmacy will provide efficient one-stop service.

To receive that care, patients will be able to choose group practice or solo practitioners.

The building itself is a monument to Dr. Sanders' determination and leadership. A hospital committee recognized in 1955 the need to replace the 1903 Outpatient Building.

As a succession of other requirements dominated the landscape, a series of General Directors had to relegate the Ambulatory Care Center (A.C.C.) to the bottom of the list. In 1973 Dr. Sanders was still new to his role as hospital leader. He resolved, however, to make the A.C.C. the top priority. Planning thus began that year.

Then a series of state government challenges intervened. Under the Massachusetts Determination of Need process, the hospital had to produce a variety of documentation. No sooner had the MGH complied with one request than the state would think of something new.

Document followed document until the bureaucratic paper filled whole drawers. To gather the information demanded, the hospital spent more than $300,000. Still the state process contravened with new challenges.

Ultimately by delaying construction for several years, the "money-saving" state process added $3½ millions of dollars in inflation costs. Through this trying time Dr. Sanders buoyed and guided his assistants. Endurance triumphed.

During the 26 years required to transform the A.C.C. into reality, time began to erode the effectiveness of some of the older of the inpatient buildings. Recognizing this, Dr. Sanders opened a $114 million fund drive last February. With about 30 percent already raised, that project is off to a good start. Eventually new inpatient buildings will replace the old just as the 1821 medical wards moved to modern two-bed quarters under Dr. Sanders.

One segment of the $114 million represents a plan to build a new research building. With some scattered exceptions, since 1951 MGH research has been scrunched into the old Edwards Research Building. A national record $15 million gift from Arthur O. and Gullan M. Wellman will in two years finance the construction of an additional research structure.

Research space is critical. But without funds to support the studies within, investigations would grind to a halt.

"For several years now," Dr. Sanders said, "it has become more and more painfully obvious that federal money to support science is growing less dependable. Yet without research, medical advances would stop."

The hospital's research community began to seek additional resources. When a potential gold mine appeared, Dr. Sanders guided and nurtured the negotiations. The result was a 10-year, $50-million-plus contract with Hoechst AG of Germany.

From the agreement will spring an entirely new department of molecular biology. With the ultimate consent of Hoechst, the agreement carefully protects the academic freedom of the MGH to carry out and publish its own

Dr. Joseph B. Martin

Joseph A. Califano, Jr., during visit to MGH while Secretary of Health, Education, and Welfare

basic research. Hoechst will use its own laboratories to convert to products the fruits of the MGH studies. Already the contract has become the model for at least one other major industrial commitment to American academia.

The patient care and research advances engineered by Dr. Sanders represents two-thirds of the MGH tripod. The remaining leg is education.

One of the dreams of Dr. John H. Knowles, Dr. Sanders' predecessor as General Director, was an MGH degree-granting authority. Dr. Sanders breathed life into that dream. A year ago this month, the MGH Institute of Health Professions opened its doors. To be granted will be master's degrees in four areas, bachelor's in two, and a graduate certificate in one. The degrees will provide students with the credentials lacking in the MGH studies the new programs replaced. In fulfilling this educational need, the MGH is the first hospital to independently establish such an institute.

Dr. Sanders toiled quietly. His achievements nevertheless attracted national attention. He was named chairman of the National Council of Health Care Technology. As the leader of a newly created body, he gave the committee a purpose and led it to studies of new technology like maternal serum alpha fetoprotein testing.

The man who created the committee was Joseph A. Califano, Jr., then Secretary of Health, Education, and Welfare. Dr. Sanders declined when Mr. Califano wanted him to become the nation's top health officer.

"He is a superb hospital administrator," Mr. Califano said in a telephone interview after hearing of Dr. Sanders' resignation. "He is very dedicated to providing quality health care but at a reasonable cost. He has been at the forefront of much of that."

One way Dr. Sanders fought rising health costs was to establish the nation's first Resource Allocations Board to consider new hospital expenditures. The board's expertise made physicians ponder before even requesting expensive technology. Dr. Sanders also encouraged service chiefs to hire fiscal experts to help govern their departments. Cost-saving self-insurance flowered too during his tenure.

If costs seemed important, the issue of compassionate health care predominated. Even before he became General Director, Dr. Sanders decided to develop an Office of Patient Care Representatives. One of the early such groups, the office has supported patients with legitimate complaints. By flagging potential difficulties, the office has prevented major problem areas from arising.

Likewise the MGH has strengthened its commitment to neighborhood health in Chelsea, Charlestown, and Revere. At the MGH itself, new units have opened in such diverse specialties as geriatrics, occupational disease, low back pain, and sports medicine.

But the name of the MGH was known well beyond Chelsea and Revere. Once the bamboo curtain lifted from China, a series of interchanges took place between the MGH and leading Chinese physicians.

Then a delegation of the most respected Chinese doctors came to the United States to study American hospitals. The doctors spent two of their five weeks at the MGH. Their aim? To build in Peking a teaching hospital the size of the MGH, the first western-style hospital in the People's Republic since the 1940s.

The man who was to lead the MGH

(Continued on Page 6)

Dr. Sanders and Dr. F. Sargent Cheever, Chairman of the Board of Trustees, with residents

Martin

(Concluded from Page 1)

ogist in Chief at the Montreal Neurological Institute.

The author of more than 130 research articles and four books, Dr. Martin is trying to develop a better understanding of how the brain works. He began his interim duties September 1.

The Search Committee, composed of Trustees, is seeking a permanent successor to Dr. Charles A. Sanders, who has become a key official of E. R. Squibb and Sons of Princeton, N.J. The Search Committee has held a number of meetings to decide on the qualities they are looking for in the individual who will become the 18th General Director since 1821 and are now discussing potential candidates. ■

Dr. Sanders Slowed Rise in MGH Costs

(Continued from Page 5)

through these and other achievements had an inauspicious beginning. When he left the cardiac catheter laboratory to head the MGH (*MGH News,* September 1972), he knew little about hospital administration. To those who knew more, he seemed inexperienced.

At his first news conference he announced he would try to lower hospital costs. He failed to realize then that the cycle of general inflation, among other factors, gave him limited power. That he slowed the rise in MGH costs was in itself a major achievement. When he left September 1, patients paid significantly lower charges than at several Boston hospitals.

Likewise Dr. Sanders wanted to leave his door and telephone line open to anyone wishing his attention. His office remained remarkably open. He did, however, soon learn to delegate the less critical matters.

"He was very approachable," said Dr. Thomas P. Hackett, Chief of the Psychiatric Service. "He was available to listen or to give advice."

Sympathetic listening was one of Dr. Sanders' strengths. He would sit through hours of dull recitation of details, offering a guideline when needed. More inclined to learn by ear than eye, he sought oral reports, absorbing information as parched earth welcomes rain.

Some six to eight months into his tenure, he had absorbed enough to take a firm grasp of the helm. Slow to make difficult decisions, he held his course once he did.

A cardiologist who continued seeing patients, he was twice asked by his colleagues to approve heart transplantation. Both times the MGH decided against. Dr. Sanders never wavered even in the face of controversy.

He survived such trials by convincing opponents that the institutional good had prevailed. In fact, he had a knack for cutting through partisan politics to seek what was right for patients. He would often listen to hours of debate until every voice was heard. Then he would offer a well-reasoned opinion that usually decided the issue.

Dr. W. Gerald Austen, Chief of General Surgical Services, joined the MGH about the same time as Dr. Sanders. Dr. Austen described Dr. Sanders as "a man of great integrity and maturity. He used a lot of diplomacy in getting people to work together. He did that in Cardiac Catheterization and when he became General Director."

Some felt that if his style had a fault, it was subtlety of expression. Dr. Sanders often declined to say "no." Instead he would speak through silence. Those who ignored the lack of enthusiasm or the frown often ended up retracing their missteps.

"Charlie is tactful, careful of other people's feelings," Dr. Hackett said. "Not hurting people is part of his style." He rarely lost his temper either at individuals or situations.

When a decision would mean hurting an individual, Dr. Sanders often delayed. Time and events sometimes relieved him of the necessity.

Dr. Sanders' warmth and boyish smile would catch off guard visitors expecting an austere New Englander at the helm of the MGH. He came to Boston from his native Texas. A trim six feet, three inches, he is handsome with his long sideburns. Even his dark pinstripe suits minus vest seem to avoid any air of formality.

"I remember going into his office to talk about serious things," said Dr. Joseph B. Martin, Chief of Neurology. "It didn't matter if I was alone or with a number of people. He would raise his feet onto a chair. He used this technique effectively to relax people, to get them to open up."

Whether employees or visiting dignitaries, people did open up. And for a less superficial reason too. Trust.

"I felt I was dealing with a square shooter," said Dr. Nicholas T. Zervas, Chief of the Neurosurgical Service. "I had confidence in him."

Dr. Sanders became General Director at a time of trial by fire for hospitals. Governmental regulators were usurping the power of hospital directors. Making even slow progress required determination and perseverance, traits that Dr. Sanders seemed to cultivate.

In their eagerness to wield an axe, regulators frustrated and defeated administrators. Many times good institutions lost ground in attempts to improve or even maintain good health care.

When the gloom was thickest, even when his own mood darkened, Dr. Sanders reached for his ultimate weapon: laughter.

"He has a marvelous sense of humor," said Psychiatry Chief Hackett. "That is very much his signature." He can turn it outward at a somber situation or inward at himself.

Dr. Sanders knew how to relax away from the hospital too. Even though he didn't leave his work very often.

He awoke at 6:30 and worked typically from 7:45 a.m. until 7:15 p.m. Then community or ceremonial activities often consumed the evening. He traveled a great deal for the hospital or for the national committees he led.

When time allowed, he escaped into a spy novel. Jerzy Kosinski is a favorite spinner of psychological novels.

Dr. Sanders announces a 10-year, $50-million-plus contract with Hoechst AG of Germany for basic medical research at the MGH.

Every spring Dr. Sanders enjoyed the physical labor of rolling the clay tennis court at his Wayland home. Neighbors used the court much more often than he. Sometimes he relaxed on a golf course driving the ball nearly out of sight. When he did take a vacation, fishing far from civilization proved a tranquilizer.

Dr. Sanders has a bemused fascination with politics and politicians. In part this interest derives from having a brother who ran for United States Senator from Texas.

Dr. Sanders worked well with national leaders because he understands them. Quietly he would advise them in health care matters, avoiding the temptation to upstage them.

Once he proposed a plan to reorganize the very essence of governmental structure. Urged by advisors to take public credit, he chose to remain the anonymous donor.

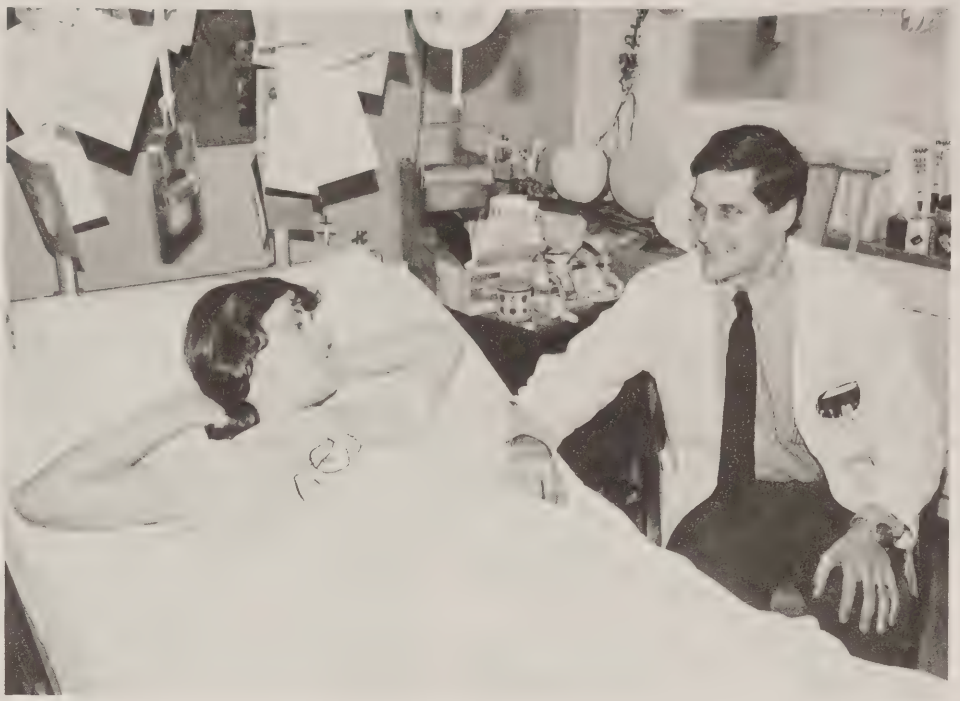
Somewhat surprisingly his quietly effective style did not escape attention. In the last few years he spurned top health jobs as widely scattered as Washington, D.C.; Texas, and California.

"People sense that he's nice as well as effective," said Neurology Chief Martin.

Another exception to the maxim that nice guys finish last. ■

Drawing shows manner in which skin and underlying tissue would be removed from a severed foot to serve elsewhere as a cover.

Mending Injuries With Salvaged Tissue



After losing her left leg in an accident, 10-year-old Karen Rousselle underwent unusual surgery by Dr. G. Gregory Gallico to be able to walk well one day with an artificial leg.

One day last April an ambulance sped from Biddeford, Me., to the MGH with a 10-year-old girl whose left leg was severed when a gravel truck hit her.

Doctors at Webber Hospital in Biddeford, where Karen Rousselle of neighboring Saco initially was taken, thought MGH surgeons might decide to reattach the limb.

Replantation was not to be. In fact, because of the extent of her injuries, Karen faced the possibility of losing even more of her left leg.

The faith of the Webber Hospital staff in the potential benefits of microsurgery, however, proved justified. With the aid of operating microscopes and the skill to rejoin the most minute and delicate nerves and blood vessels, an MGH surgical team salvaged vital parts from Karen's severed limb and used them to save her knee.

Not only did the surgeons make further amputation unnecessary, they also gave Karen hope that one day, with the assistance of an artificial limb, or prosthesis, she would walk again, and walk well.

The head of the operating team, Dr. G. Gregory Gallico of the Plastic Surgical Division, first examined the girl in the MGH's Emergency Ward.

"To replant her leg we would have had to shorten it six or eight inches because of severe muscle damage," he said. "That would have been worse than having no leg at all. Karen would be much better off with a well-designed, lightweight artificial limb."

With her leg cut off at mid-calf, she retained her knee joint, and below her knee was a four- or five-inch length of bone which could fit into a prosthesis to help activate it.

But there was no skin. It had peeled off in the accident from the left thigh all the way down. Although still functional, the knee joint was thus bare. The bone below also lay exposed. Unless surgeons could take corrective steps, they would have to amputate at the mid-thigh.

Without her knee even the best prosthesis would permit but a poor gait. To walk, she would have to swing the entire hip, expending much more energy than normal knee action would demand.

"The foot attached to the severed leg was still in good condition," Dr. Gallico said, "so we decided to remove from the foot all of the skin as well as underlying muscle, fat, nerves, and blood vessels. We would then have the ingredients to fashion a new cover, or flap, of both skin and soft tissue to protect

(Concluded on Page 8)

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Reuse of Tissue Saves Injured Girl's Knee

(Concluded from Page 7)

Karen's thigh, knee, and leg bone."

The transplanted veins and arteries would assure a life-preserving blood supply for the flap, and the nerves would restore sensation in the treated leg.

Only an hour or so after the girl's arrival at the MGH, the surgery began. It lasted eight to ten hours. Assisting Dr. Gallico were Drs. Frederick N. Lukash, also of plastic surgery; Houston Johnson, Jr., of pediatric surgery, and Jesse B. Jupiter of orthopedic surgery.

The operation went well. Three days later, however, a clot developed in one of the newly connected blood vessels. Back in the operating room, Karen underwent a vein graft to bypass the clot.

"We would have lost about half the flap if the procedure had failed," Dr. Gallico declared. "But it was successful."

The fifth grader, who was the only girl player on a Little League baseball team in Saco, at first had trouble adjusting to the loss of her leg, but she has now accepted the handicap. "It's difficult to assess how deep that acceptance goes," Dr. Gallico said, "but Karen is a very mature child."

Because of the skin loss, Karen has injuries that in many respects resemble those of a burn patient. Consequently, she makes periodic visits to the MGH-affiliated Shriners Burns Institute for her rehabilitation management. Dr. Gallico, who is also on the Shriners' staff, continues to supervise her care.

"With proper physical therapy," he said, "we should be able to restore very good knee function, then fit her with a prosthesis, and train her to use it. Barring the unexpected, she should be able to walk well in about a year."

The doctor based his optimism in part on the success of the leg procedure at Jewish Hospital in Louisville, Ky., where two boys, aged 9 and 10, were so treated, and at New York University Medical Center, where an 18-year-old girl underwent similar surgery.

However, tissue salvage is not limited to leg repairs. Two years ago, MGH doctors used salvaged materials to preserve the left elbow of a 21-year-old mentally unstable man. He had deliberately severed his left forearm.

In an article published in *The Journal of Hand Surgery*, the surgeons described how they at first contemplated a replantation but ruled it out after conferring with psychiatrists who studied the patient.

Dr. James W. May, Jr., Chief of Hand Surgery in the Plastic Surgical Division, said the psychiatrists advised against a replantation because it would have taken a long time for the patient to regain full sensation in his arm, and the wait would normally be an ordeal for even the most stable individual.

Frequent chats with Ann Gerberg, RN, helped to quicken Karen Rousselle's recovery.

The amount of tissue remaining below the patient's elbow was insufficient for a proper stump closure, thus raising the apparent need for an amputation above the elbow. But Dr. May and his team, including Drs. Reid H. Hansen of plastic surgery and Lee Gordon of orthopedic surgery, turned for additional material to the hand on the lost arm.

From the entire palm they removed the skin along with underlays of muscle, fat, blood vessels, and nerves. They then moved the flap to the forearm stump. The surgeons were able to cover not only the elbow but also a three-inch length of forearm bone which could provide leverage in future use of an artificial arm.

Six weeks later, the young man could fully move his elbow, and the fitting of a prosthesis began.

The MGH became involved early in the concept of tissue salvage. In August of 1976, Dr. May and Dr. Richard J. Smith, Chief of Hand Surgery in the MGH Orthopaedic Service, operated on a 10-year-old boy born with clawlike feet and no thumbs. The surgeons transplanted the youngster's big toes to serve as thumbs, then remodeled the feet so that he could walk more normally.

Since that time, the MGH has performed 18 toe-to-hand transplantations.

"Before the advent of microsurgery," Dr. May declared, "needed tissue was often available, but there was no effective way to transfer the material from point A to point B.

"Microsurgical techniques have not only solved this problem but have also focused much attention on the many potential uses for salvaged parts of the human body." ■

MGH News

Vol. 40 No. 7 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS October, 1981

Combatting Bulimia, a Secretive Craving for Food

Special Laboratory Helps to Identify Odd Organism

Recently, a team of medical researchers reported a study to determine the prevalence of sexually transmitted conditions among several hundred women attending a large American university.

In the article in the *American Journal of Obstetrics and Gynecology,* the investigators revealed that while only two (.4 percent) of the students had gonorrhea, ten times that number had a venereal infection caused by another microorganism known as *Chlamydia trachomatis.*

The finding by the team, directed by Dr. William M. McCormack of the Channing Laboratory of Harvard Medical School and Massachusetts State Laboratory Institute in Boston, underscored increasing concern over a nationwide problem of epidemic proportions.

The problem has also become linked with a number of medical conditions of previously unknown cause.

High on the list is a form of infant pneumonia. Each year in this country, more than 150,000 babies contract chlamydial infections at birth from their mothers, and 30,000 of these infants develop pneumonia, usually between four and 18 weeks of age. The disease responds well to the antibiotic erythromycin.

Since Chlamydia trachomatis *is an organism of unusual composition and causes genital, lung, or eye infections*

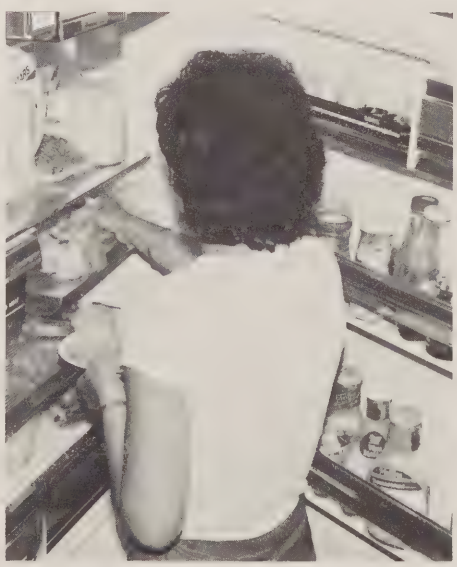
(Continued on Page 4)

For the most part they seem perfectly normal. On an average in their mid-20s, vigorous, healthy-appearing, intelligent, successful, the patients present a picture of general well-being.

No one would ever imagine that as often as several times daily these individuals, mainly women, gorge themselves on food, consuming as much as $70 worth per day. They tend to choose foods that are easily chewable and high in calories.

Why don't their bodies reflect their insatiable appetites?

Between the eating binges, the patients, feeling pangs of shame and guilt, deliberately seek quick relief. They empty their systems by inducing vomiting or by gulping laxatives. Some MGH patients have admitted taking up to 300 laxatives weekly for five or six years before seeking treatment.



Persons with bulimia indulge in repeated eating binges.

Physicians refer to the condition as bulimia (from Greek words meaning ox and hunger). *Bulimia used to be considered rare, but now some medical investigators estimate that as many as one out of every five women at America's colleges engage to some degree in the so-called "binge-purge" syndrome.*

At the MGH, an Eating Disorders Clinic has been organized, utilizing the services of many types of specialists. The clinic is the first outpatient evaluation and treatment center of its kind in New England.

Eighty percent of the patients suffer from bulimia. The rest are afflicted with anorexia nervosa (*MGH News,* October 1976), a psychiatric disorder in which an overwhelming desire for thinness leads to an aversion to food.

On occasion, an anorectic will go on a binge, consuming heaping amounts of food and then, as in bulimia, self-induce vomiting.

Established under the Psychiatric Service, the Eating Disorders Clinic is directed by Dr. David B. Herzog, who is both an adult and child psychiatrist and a pediatrician.

Other clinic staff members and their specialty include Dr. Nancy Rigotti, internal medicine; Dr. Joan F. Mansfield, pediatrics and reproductive endocrinology; Theodore McLaughlin and Dale Sokoloff, psychology; Ruth Palombo, nutrition; and Carolyn Sprich, social work.

Much has been written in medical and lay literature about the anorectic, whose weakened body provides visual

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114
Telephone (617) 726-2206

Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD

Joseph B. Martin, MD, *Interim General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIAL:

Saving Force Or Corrupting Influence?

Industrial support of academic research: saving force or corrupting influence? A decade ago the concept of industry funneling money into academia's laboratories was an imaginative idea, little more. Suddenly, though, industry is bestowing millions of dollars on university and hospital research.

Two major forces have impelled this series of actions. First came the technological explosion in genetics. Whether in science columns or the business page, it is becoming difficult to find a newspaper that fails to mention "gene splicing" or "monoclonal antibodies." These techniques promise major advances in medical care, not today but in the future. With breakthroughs, ultimately come profits to industry. That explains the industrial compulsion to invest in these studies.

The second major force behind the recent incursion by industry is Washington's tendency to provide fewer dollars for basic research. Given this trend, biomedical researchers are likely to continue to accept industrial support. With promising improvements in health care the likely eventual result, this course has a firm foundation.

Is there a danger of industrial dollars unduly influencing academia? Yes. Such a threat exists whenever large sums are involved. Twenty-five or so years ago the same questions were being asked when the federal government began giving millions for academic research. What has since evolved is a careful system established to safeguard the research from many standpoints including academic freedom.

Today most knowledgeable people would agree that on the whole the system works well. Now that industry's dollars have appeared, academia has to be equally vigilant in protecting its freedom from the new source of funding. To guard academic research, guidelines seem in order. In fact, the MGH Board of Trustees has established a committee to advise on the question of guidelines. And in December, the trustees' Scientific Advisory Committee of leading non-MGH scientists will examine the question of science-industry cooperation. It was in 1975 that the Scientific Advisory Committee initiated discussions of that topic.

One can never guarantee the long-range results of this growing relationship with industry. What provides a strong measure of reassurance, however, is the considerable concern exhibited from within the academic community. Just as such concerns helped establish an accepted relationship with government, they bode well for future contacts with industry. But academia and industry must *remain* vigilant.

Bulimia Often Stems From Episodes Of Stress

(Continued from Page 1)

evidence of her plight. Bulimia, however, remains a clouded entity.

Unaffected by wide fluctuations in weight, the bulimic individual can easily conceal the uncontrollable, behind-the-scenes preoccupation with food.

"I treated one bulimic patient who kept her condition secret even from her spouse during 20 years of marriage," Dr. Herzog said.

Usually among the better-educated and from well-to-do families, persons with bulimia often struggle to solve their difficulties themselves rather than reveal their embarrassing behavior, even to a physician.

What precipitates bulimia? It occurs most often in obsessive, perfectionistic people who are dealing with stresses in their lives. These stresses can be secondary to internal conflicts or external pressures and may often involve ambi-

Photographs: Myron Daniels
Drawing: Page 7, courtesy of Dr. Roberto C. Heros.

Change of Address

If you have moved, or your name or address is incorrectly listed, please clip out this form and print or type correct address below. Zip code must appear. Kindly enclose address label from back page.

Name (Please Print or Type)

Street Address

City *State* *Zip Code*

AFFIX OLD ADDRESS HERE

Please mail to:
News Office
Massachusetts General Hospital
Fruit Street
Boston, Mass. 02114

valent feelings.

Dr. Herzog said episodes of binge-purge eating may occur after a death, divorce, separation from home, a career decision, or a breakup with a close friend.

He told of a 20-year-old bulimia patient who had taken 40 laxatives a day for five years. The root of her problem: a strained relationship between her parents. Her illness diverted the attention of the parents from each other to her and thus kept the family united. Under treatment which included outpatient group therapy and brief inpatient care, the patient has managed to virtually halt her ingestion of laxatives.

Another patient, a young man, developed bulimia after going off to medical school. Ever dependent on his family for decision-making, the student became uncertain about his career goals. He felt the course of his life had strayed beyond his control.

Food tended to dispel the concerns and make up for feelings of loneliness and boredom. The inevitable sense of shame and low esteem followed. Then, laxative abuse, eight to 10 pills a day.

"None of these people can really enjoy a meal," Dr. Herzog said, "because, fully aware of what they are doing, they worry about body image. Depression almost always sets in during or after each binge."

Under treatment designed to bolster his self-esteem, the medical student has stopped his impulsive eating and overuse of laxatives, but he still fears the addiction may recur.

Thinking of their strange eating activity, many bulimia patients suspect that they are out of their minds. "They are not," Dr. Herzog emphasized. "There is a reason for their particular behavior. During treatment, patients have the opportunity to become aware of the rationale behind their conduct."

Patients are referred to the MGH Eating Disorders Clinic by other clinics, hospitals, private physicians, and lay organizations, such as the Anorexia Nervosa Aid Society of Massachusetts (A.N.A.S.).

Financial support for the clinic comes in part from A.N.A.S. in the form of a three-year, $50,000 grant in memory of the late Abigail Adams Atchley. The grant was established through her father, Dana W. Atchley, Jr., a founder and director of A.N.A.S. and a senior executive of M/A-Com, Inc.

Because bulimic individuals resist telling anybody about their problem, care givers move cautiously. Dr. Herzog, an Instructor in Psychiatry at Harvard Medical School, declared, "We can't impose our services. We have to be flexible, determining first what the patient can tolerate."

Initially, a patient may derive the most benefit by seeing a nutritionist on a weekly basis or an internist on a biweekly or monthly schedule.

In time, the trusting relationship spawned by this supportive counseling may expand to include the psychiatrist. He can then initiate formal psychotherapy (treatment by oral communication that may embrace suggestion, persuasion, reeducation, or reassurance).

Some patients feel so alone with their problem that participation in group therapy proves to be the best course. The Eating Disorders Clinic works closely with A.N.A.S., which sponsors self-help, group programs, directed by recovered anorectic or bulimic individuals.

"Some patients can tolerate only an association with a friendship-type group," Dr. Herzog said. "We may see these people once every four or six weeks for follow-up."

Since the causes of bulimia often arise from family relationships, the psychiatrist may seek to counsel the family as well as the patient. Helping parents to readdress their own lives can sometimes open the way to solving an offspring's dilemma.

The Eating Disorders Clinic staff meets every week to discuss patients and treatment programs. Patients visit the clinic on Wednesdays. Evaluations for one person take several hours and range from psychological testing to physical examinations, depending on the patient's willingness to cooperate.

Dental problems sometimes result from the dehydration and acidity caused by frequent throwing up. Thus, at the MGH an oral surgeon may be asked to examine a bulimic patient. Some have sought care at the clinic only after having had all their teeth capped. They had never told anyone, even their dentist, about their eating habit.

Depending on how much vomiting they do, some patients suffer from loss of potassium needed for proper heart and kidney function. In situations involving laxative abuse, the clinic will check on possible loss of calcium, important for sound bones and a multitude of other roles in the body.

Reports in the literature tell of bulimic persons developing a swelling of the parotid glands. These are large salivary glands found near each ear. Parotid swellings are a common sign of the mumps. Why the change occurs in bulimia is unclear.

With the widespread incidence of bulimia increasingly apparent, health professionals are paying more attention to the disorder, but there is much for them to learn. The nature and effectiveness of treatment hinge on the frankness and cooperation of those stricken by the problem. ■

Bulimic individuals commonly sneak food to a bedroom or bathroom so as not to be caught eating extra meals.

An Agent That Displays Peculiar Traits

Using an inverted microscope in the Chlamydia Laboratory, Consultant Teresa Rota monitors the growth of tissue cells to be used for the isolation of chlamydiae.

(Continued from Page 1)

in well over two million Americans each year, to help diagnose the illness the MGH has opened a special Chlamydia Laboratory in its Infectious Disease Unit.

Dr. Martin S. Hirsch directs the laboratory. Sarabelle Madoff is chief technician, and Teresa R. Rota, who has conducted research on chlamydiae at the Harvard School of Public Health, serves as consultant.

Dr. Hirsch, who also supervises the MGH Virology Laboratory, said that chlamydiae are unusual in that they bear almost all the features of bacteria but lack some biochemical pathways needed to make energy. Therefore they must grow, like a virus, in a tissue cell.

Two species of the organism are known. In addition to *Chlamydia trachomatis*, there is a form called *Chlamydia psittaci* which causes psittacosis, or parrot fever. This disease, carried by birds, is relatively rare, striking only about 1,000 persons annually in the United States.

To diagnose a chlamydial infection, the laboratory cultures the organism as if it were a virus. Treatment, however, calls for antibiotics, drugs to which viruses are insensitive.

The name chlamydia comes from the Greek word *chlamys,* meaning cloak. When stained and then viewed under a microscope, the organisms take on a cloak-like appearance near the nucleus of the cell.

In women, the infection may initially inflame the cervix, the neck of the uterus, then progress to an inflammation of the fallopian tubes. The condition, known as salpingitis, can ultimately lead to infertility.

Infected newborns pick up the disease during vaginal delivery. In addition to pneumonia they may develop conjunctivitis, an inflammation of the inner surface of the eyelid and exposed surface of the eyeball.

In men, *Chlamydia trachomatis* infection often appears in the form of a nongonococcal urethritis (NGU), an inflammation of the canal (urethra) through which urine is discharged. Symptoms such as burning discomfort during urination may not appear until a few weeks after relations with an infected partner. Her illness may go undetected for a much longer period and even be missed entirely.

Microscopic view of chlamydiae

Studies indicate that chlamydiae cause 40 to 50 percent of NGU episodes. Sometimes a male will contract both gonococcal urethritis and NGU at the same time. Upon discovery of the gonococci, physicians usually prescribe penicillin, but the drug will not combat the chlamydiae. If the urethritis persists or recurs, and gonococci are no longer present, tetracycline can be an effective remedy.

Chlamydial infection in males can lead to a complication called epididymitis. This is an inflammation of a cord-like structure situated next to the testicle. The epididymis provides a storehouse for sperm and forms part of the duct through which sperm travels from the testicle. Although an important condition, epididymitis is fairly uncommon.

Dr. Hirsch, who is also Associate Professor of Medicine at Harvard Medical School, said he does not encourage universal culturing for chlamydiae because the procedure is expensive.

"Tetracycline and erythromycin have proved to be so effective against chlamydiae," he said, "that if presence of the organism is suspected, we will often advise giving the medication right away to see if the condition abates."

He said, however, that certain specimens, such as from surgical patients or from infants stricken with pneumonia, should be sent to the laboratory for analysis.

"In these kinds of situations," he declared, "it is especially important to have a very clear picture of the patient's condition before determining treatment. We may be dealing with several disorders, each requiring a specific action."

A type of *Chlamydia trachomatis* similar to the organism responsible for conjunctivitis is the leading cause of preventable blindness in the world. The disease that is produced is called trachoma. It is particularly common in Africa, Asia, and Latin America, but it has also been found among Indian tribes in parts of the southwestern United States.

"The threat of blindness arises primarily in those areas of the world where children are exposed constantly to trachoma," Dr. Hirsch said. "Treatment may bring results, but two weeks

later the infection is back."

Psittacosis, caused by *Chlamydia psittaci,* has become more prevalent in this country over the past few years, and Dr. Hirsch offered two possible reasons: increased interest in parrots and parakeets as pets and less than adequate quarantine measures.

The doctor said the law requires imported birds to be quarantined for a month. During that time they are supposed to receive a diet containing tetracycline. "Unfortunately, some of the birds fail to receive the prescribed diet," Dr. Hirsch declared. "And more often than not, those birds that have become infected show no indication of illness."

He deplored "parrot fever" as a term to describe psittacosis because virtually any bird can be a carrier of the organism. Health officials have reported outbreaks among workers handling turkeys and ducks in slaughterhouses.

The infection, which can on occasion spread from person to person, causes a flu-like syndrome but can progress to a severe pneumonia. Fever may persist for two or three weeks. In a quarter of the patients no exposure to birds can be documented.

The incidence of psittacosis is dwarfed, however, by the numbers stricken in one form or another by infection with *Chlamydia trachomatis.*

"More and more diseases of the male and female genitourinary systems are being recognized as caused by chlamydial infections," Dr. Hirsch declared. "The MGH Chlamydia Laboratory is one of a relatively few around the country, but the number is increasing as the chlamydia organisms become better known and their significance becomes more apparent." ■

Sarabelle Madoff, Chief Technician in the Chlamydia Laboratory, inoculates tissue cells with specimens suspected of harboring the unusual organism.

When Turnabout is Fair Play

In a setting such as the MGH's Cox Center, which brings together medical oncologists, surgeons, radiologists, and pathologists, the radiation specialist joins in proposing and discussing alternative approaches for cancer treatment.

Not infrequently, a switch of sequence—having radiation precede surgery—has spelled the difference between success and failure in curing patients with malignant tumors.

About five years ago, for example, an attractive 27-year-old woman was admitted to the MGH suffering from a nearly four-inch growth in her left calf. The tumor was a type of sarcoma which develops from cells of connective tissue.

Surgeons felt the tumor was inoperable because of its advanced state, thus raising the probability of an amputation of the leg above the knee. However, the surgeons asked the radiation specialists if they could save the leg.

After determining that the disease had not spread from the primary growth, the therapists administered radiation treatments that shrank the tumor to less than two and a half inches in diameter and also killed virtually all of the malignant cells.

Three weeks later surgeons removed the tumor. The radiation therapist implanted a series of tubes (catheters) in the tumor bed. They subsequently were loaded with a radioactive material (iridium) to further treat the disease.

For two years after that, the patient took various medications, but since terminating the drugs more than three years ago, she has undergone no further treatment. She is disease free, works, and enjoys a perfectly normal life.

An MGH team led by Dr. Herman D. Suit, Chief of Radiation Medicine, has studied the effectiveness of preoperative radiation treatments on 63 patients afflicted with sarcomas of soft tissue, i.e., in fatty tissue, muscles, lining of joints.

"Surgical colleagues have judged our results to be most encouraging," Dr. Suit declared.

Of the 63 patients studied, four failed to benefit from radiation followed by surgery. Dr. Suit said all four had very advanced tumors which regrew despite the treatment.

For three other patients, surgeons had to call off operations because the tumors had major vessels passing through them. Radiotherapists completed the treatment, but the disease spread.

"We do not have a treatment that is 100 percent successful," said Dr. Suit. "But for most tumors which are clearly operable, we appear to be achieving our goal: prevention of local recurrence and retention of good function and appearance of the affected part."

Sarcomas represent only about one percent of the malignant diseases in the American cancer population. About 4,500 soft tissue sarcomas and 1,900 bone sarcomas are reported annually in this country.

Most cancers are classified as carcinomas. These consist of cells (epithelial) found in the skin and in the

(Continued on Page 6)

Tumor Care May Hinge on Growth Site

Dr. Herman D. Suit prepares patient for cobalt radiation treatment of thigh tumor.

(Continued from Page 5)

covering of most internal organs and cavities of the body.

Dr. Suit said that sarcomas of soft tissue, which represent his area of special interest, occur most often in the extremities, and he added, "We think radiation therapy has an important role in quite a high proportion of such patients."

Sarcomas also arise about the head and neck, in the shoulder area, and on the torso, particularly the buttocks region.

The most difficult sarcomas to treat are those which develop in the back of the abdomen (retroperitoneal area). "These tumors are usually large when first seen, and the structures they invade preclude any adequate surgical resection [removal]," Dr. Suit explained.

"The tumors are also in an area where the surrounding normal tissues are quite sensitive to radiation. High doses are not feasible."

Sarcomas occurring in persons under 20 years of age usually arise in muscle (rhabdomyosarcomas) and can be treated successfully with surgery, high-dose drugs (chemotherapy), and radiation. The radiation may turn out to be unneeded.

No one knows why other types of sarcomas are seen predominantly in patients older than 20. Some of the diseases are believed connected with genetic disorders. For instance, physicians sometimes detect tumors called neurofibrosarcomas in patients with neurofibromatosis (*MGH News*, October 1980), the condition which plagued the central figure in the drama, "The Elephant Man."

In giving preoperative radiation treatment, MGH technicians in the Cox Center use a cobalt unit to administer small daily doses of 200 rad (a rad refers to each unit of energy absorbed from the machine's beam per gram of tissue). Delivered five days per week, the treatment extends over five and a half weeks, followed by a two- to three-week rest period and then surgery.

Radiation Therapy Technician Paul Van Ocken controls operation of cobalt unit.

During the operation, the tumor area receives a boost dose of 1,000 to 1,400 rad. Thus, the total normal dosage per patient will be in the order of 6,600 to 7,000 rad, depending on the circumstances. If treatment cannot be accomplished in part with surgery, the radiation that is given may total 7,500 to 8,500 rad.

Reporting last May in the scientific journal *Cancer* on earlier progress of the sarcoma studies, Dr. Suit and his colleagues wrote that preoperative radiation goes beyond shrinking a large cancer, thus making it possible in most instances for the surgeon to apply his skills. The radiation also eradicates microscopic extensions of the growth beyond the obvious malignancy.

Also, they pointed out, if radiation exposure were held up until after surgery, the patient would be subjected to treatment of a larger volume of tissue. The areas to be treated would have to include not only tissues suspected of involvement with the tumor but also all tissues manipulated or handled during the surgical procedure.

In the article, coauthored by MGH Drs. Karl H. Proppe, of Pathology; Henry J. Mankin, Chief of Orthopaedics; and William C. Wood, a surgical oncologist who is Medical Director of the Cox Center, the issue of wound healing also was brought up.

The doctors stressed that if treatment begins with surgery a two- to three-week period must elapse to allow the wound to mend before the start of radiation. During the wait, any tumorous material remaining in the wound would continue to grow.

Dr. Suit said in an interview that by radiating first "you're killing off nearly all of the tumor cells. Most die within the first week or two of treatment. The remainder of the radiation treatment is aimed at getting rid of the last few cells. So there is no harm in delaying the start of surgery."

Preoperative radiation may not be advisable, however, if the cancer lies close to some critical structure where any problem in wound healing would pose a serious threat.

A specialist at St. Vincent's Hospital Tumor Clinic in Sydney, Australia, Dr. Leicester Atkinson presented the earliest scientific paper on the preoperative radiation concept in 1963. Dr. Suit's

Nerve Disorder Tests Human Endurance

Sketch depicts area where neurosurgeon conducts brain operation to end pain of trigeminal neuralgia.

One night late in the year 1677 an English physician in Paris hurried to the home of his country's ambassador whose wife was suffering excruciating pain.

When Dr. John Locke came upon the Countess of Northumberland, she was crying out from what she later said were flashes of fire engulfing the entire right side of her face and jaw. Twitches distorting the face accompanied each spasm of pain.

Suddenly the attack ceased and except for a slight throb in her jaw the Countess once again seemed perfectly well. But this was not to last. Hours afterward, the torment returned.

In a letter to a friend and medical colleague, Dr. Locke related how speaking, eating, or just touching the right side of the face often gave rise to the attacks. Various treatments, such as the vigorous use of cleansing laxatives and applications of pain relievers to the gums, failed to provide any durable comfort.

Dr. Locke's detailed account of his patient's condition is believed to be the first description by a physician of an illness known today as trigeminal neuralgia. The term means sudden spasmodic or convulsive pain along the trigeminal nerve which transmits sensation from the face to the brain. Another name for the malady is tic douloureux, a French expression meaning "painful twitching."

"This is one of the most painful conditions that a person can have," said Dr. Charles E. Poletti, Director of the Neurosurgical Pain Unit at the MGH. "It is fortunate that as a rule each episode of pain lasts only a few seconds or minutes. A longer attack would probably be unbearable."

Even after a person is again pain-free, the patient lives in dread of his next attack. Dr. Poletti said that although pain-free periods are common, permanent remissions are not unless medical attention has been provided.

A breath of wind on the face, a smile, a turn of the head, or changing one's position in bed may be sufficient to activate so-called trigger points in the face and bring on the distress.

Ironically, between periods of susceptibility to attacks, a person may touch or press upon known trigger zones and suffer no pain at all. Doctors cannot explain this.

Each year in the United States trigeminal neuralgia strikes an estimated 15,000 persons for the first time. Many, thinking they have a violent toothache, turn first to a dentist. The neuralgia closely resembles the sharp ache one can get from the exposed nerve of a tooth.

Finding no dental problem, today's more sophisticated dentist will realize the possible presence of trigeminal neuralgia and refer the patient to a neurological specialist.

Two drugs frequently prescribed for epilepsy are also widely used to treat trigeminal neuralgia. They are carbamazepine (Tegretol) and diphenylhydantoin (Dilantin). However, although each may be helpful at first in controlling painful attacks, for many patients the two medicines ultimately lose their effectiveness.

Increased dosages of the drugs may produce unwanted side effects. Too much Tegretol causes sedation and mental sluggishness. Excessive Dilantin can lead to difficulties with balance.

In those patients in whom medical treatment has failed, an alternative is surgery.

Not very many years ago the only operative solution was to sever the trigeminal nerve. While this disposed of the agony, the surgery also left the face completely numb.

About 14 years ago, Dr. William H. Sweet, then Chief of Neurosurgery at the MGH, introduced a new technique designed to stop the pain but preserve sensation. The procedure won quick adoption.

The treatment involves insertion of a special needle-electrode into the cheek. Contacting the trigeminal nerve

(Concluded on Page 8)

interest in the procedure began a few years later while he was at M. D. Anderson Hospital in Houston. He introduced the preoperative radiation approach in that center in 1967.

Dr. Suit recalled that one of the first two patients was an architect in his early 30s who had a very large thigh tumor that was believed inoperable. Under radiation, the growth decreased in size from nearly eight inches to a little more than three inches. When a surgeon removed the remaining mass, pathologists could detect no live tumor cells.

Dr. Suit continued to employ and study this combination approach after joining the MGH in 1970.

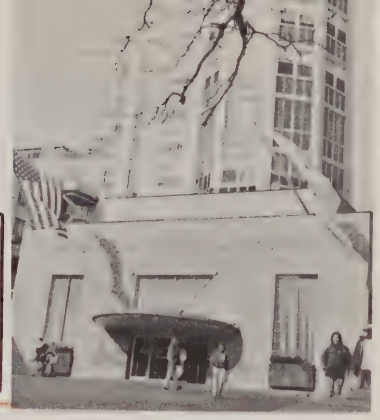
"The preoperative radiation scheme offers a very major advantage for patients with large or difficult lesions," he said. "The surgical procedure can be made more conservative and more readily tolerated by the patient. I think this is clearly a more effective strategy than the traditional approach of operating first."

The MGH Chief of Radiation Medicine and Professor of Radiation Therapy at Harvard Medical School added, however:

"This is an opinion from a person who is a bit of an enthusiast. To prove the point, what we really need to do is to study patients in greater numbers and for longer periods of time." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416



Painful Nerve Condition Yields to Surgery

(Concluded from Page 7)

at a point within the skull but outside the brain, the surgeon uses his instrument, heated to various degrees, to burn away pain-causing fibers while leaving other fibers of the nerve relatively undisturbed. To determine during surgery whether or not the pain fibers from the painful areas have been destroyed, the doctor pricks various parts of the patient's face and asks whether any sharpness is being felt.

Dr. Poletti, who trained at the MGH under Dr. Sweet, has operated on 150 trigeminal neuralgia patients, primarily using the Sweet method. For the others, surgeons employ a technique designed by Dr. Peter J. Jannetta, Chairman of the Department of Neurological Surgery at the University of Pittsburgh School of Medicine.

This procedure is used by Dr. Poletti and by Dr. Roberto C. Heros, Director of Vascular Neurosurgery at the MGH. Dr. Heros learned the technique while working with Dr. Jannetta at Presbyterian-University Hospital in Pittsburgh. It is a major operation, requiring special training for the neurosurgeon.

The operation is performed in an area of the brain loaded with important structures of the nervous system and leaves no margin for error.

The surgery, called a microvascular decompression, counters what some believe to be the principal cause of trigeminal neuralgia, namely pressure of a brain artery or vein upon the trigeminal nerve. The pressure can develop during the aging process as arteries and veins elongate and the brain tends to sag. The neuralgia most commonly arises in individuals beyond 50.

The Jannetta technique aims at repositioning the blood vessel that is pressing on the nerve. The pain would thus cease, and there would be no threat of numbness. Dr. Sweet's operation sometimes leaves numbness.

Dr. Poletti pointed out that without feeling in the face a person could get something on the cornea of an eye and not realize it until ulcers had developed. In rare instances, this has led to loss of sight.

The doctor also said a very small percentage of patients insist they would prefer continued pain to a postoperative lack of facial sensation.

The brain area considered most vulnerable to blood vessel compression upon a nerve is known as the cerebellopontine angle, situated near the brain stem which connects the brain and spinal cord.

The surgeon must work through a silver-dollar-sized hole, drilled near the lower back of the patient's skull, and must use a microscope and special instruments to manipulate the delicate brain structures.

Dr. William H. Sweet, developer of a technique to relieve trigeminal neuralgia

Dr. Poletti, who is also Assistant Professor of Surgery at Harvard Medical School, said the microvascular decompression may be the ideal procedure for the trigeminal neuralgia patient who is under 65 years old and in generally good medical condition.

For the patient over 65 who may have problems such as a heart condition, diabetes, or high blood pressure, the neurosurgeon recommends Dr. Sweet's technique, known as a percutaneous (through the skin), radiofrequency rhizotomy.

"It is certainly safer, and it can be repeated, if necessary," Dr. Poletti declared.

He estimated the risk of death in the open operation at a little less than one percent while loss of life from the rhizotomy would be extremely rare. The open surgery would require a week in the hospital compared to a less costly overnight stay for the rhizotomy patient.

Some people have redeveloped neuralgia after a microvascular decompression. This usually occurred less than a year after the operation because of some technical factor: an artery moving back to where it had pressed against the nerve, or the dissolving of a sponge placed to separate an artery and a nerve.

In such circumstances, Dr. Poletti said he would not repeat the Jannetta technique but would turn to the safer procedure.

The doctor reported that if a patient went pain-free for a year after undergoing a microvascular decompression he usually remained free of pain.

"Each operating method has its advantages," Dr. Poletti said. "I think the surgeon should fully inform the patient about both strategies and then, if possible, let him make the ultimate choice." ■

MGH News

Vol. 40 No. 8 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS November, 1981

A Familiar Hormone Exhibits Links With Memory

Patients Can Prove Less Than Candid

Why do people go to doctors? Obviously to have them diagnose and treat sickness or injury.

Perhaps not so obvious.

Many visits to physicians' offices appear to be motivated by other factors, and often a doctor becomes something of a sleuth to ferret out the real reason for a patient's coming.

Studies indicate that during a two- to four-week period, three-quarters of the general population experience symptoms they associate with illness or injury, but only 25 percent or so see the doctor.

Usually, an individual will dismiss fatigue as due to insufficient sleep, a backache as the result of sitting or lying in the wrong position, or a gnawing

(Continued on Page 4)

Investigators probing the workings of the mind may be getting closer to unraveling one of the brain's most complex puzzles: how a living being remembers.

A number of research groups, including one at the MGH, is studying a chemical substance called vasopressin, which originates in the brain.

Vasopressin has long been known as an antidiuretic hormone because it acts in the kidneys to conserve body water. By stimulating the contraction of muscular tissue in blood vessels, the hormone also raises blood pressure.

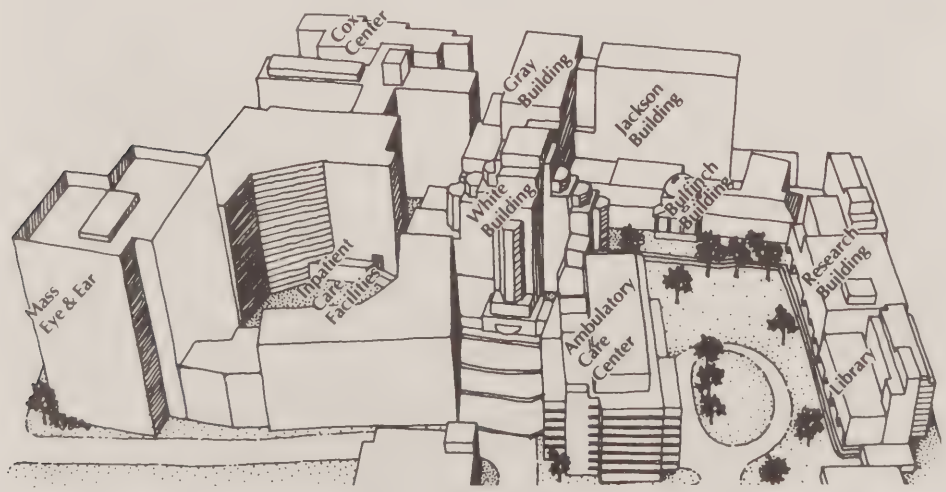
In recent years scientists have become aware of another function of vasopressin. Circulating in cerebrospinal fluid (CSF) which gives the brain protective buoyancy, the hormone has been shown to affect learning and memory in animals.

Dr. Steven M. Reppert, a pediatrician in the MGH Neuroendocrine Research Laboratory, advanced the investigation another step. He found that vasopressin concentrations in CSF continuously withdrawn from free-ranging cats exhibited a large daily rhythm and that the highest concentrations occurred during daylight hours. The hormone, or peptide, displayed no such pattern in blood circulation.

Writing in the September 11th issue of *Science,* Dr. Reppert suggested that the rhythmic changes of the chemical in CSF further implicate this body fluid as a vehicle of communication within the brain. He said these changes provide additional evidence that vasopressin may act by means of the cerebrospinal fluid to influence behavioral processes, such as memory.

Coauthors of the article were Drs. Henry G. Artman, Subbiah Swaminathan, and Delbert A. Fisher of the Harbor-U.C.L.A. Medical Center in Torrance, California. They assisted in the project by measuring the vasopres-

(Continued on Page 2)



A proposed new look for the MGH

Planning for Future Health Care Needs

During 1822, its first full year of operation, the MGH admitted a grand total of 115 patients.

The hospital's original structure, the Bulfinch Building, still sat incomplete on a four-acre pasture lining the Boston bank of the Charles River.

Not until 1823 did workers apply finishing touches to the imposing granite-block edifice, bringing it to a planned 73-bed capacity.

No one doubted, however, that the future of the first voluntary, general hospital in New England and the third

(Continued on Page 7)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, MA 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
Joseph B. Martin, MD, *Interim General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIAL:

So What's Wrong With $50 Million?

When is a $50 million-plus "gift" a hindrance? When it hinders the recipient from obtaining donations desperately needed for other purposes. The "gift" in the riddle is really not a gift but the money an international chemical firm named Hoechst AG has agreed to pay the MGH for carrying out important research. Specifically the funds go to one research department of the hospital. And the studies offer tremendous potential benefit to patients all over the world.

So what's the problem? It stems from a public misconception. Many people believe that the $50 million-plus will become part of or otherwise benefit the hospital's $114 million capital campaign. None of that Hoechst money can or will. As a page 1 article points out, the $114 million drive does have nearly $38 million of its own. Only a small percentage of that sum, however, has been designated by donors to replace patient care beds. Yet $85 million of the $114 million is needed to replace inpatient areas that are growing significantly outdated.

One might well ask why the *MGH News* is delving into this problem. When the *News* in its present format began 13 years ago, it was dedicated to informing its readers about the major health care advances. More recently this publication has added articles about maintaining health. Since its rebirth in 1968 the *News* has consciously avoided articles about fund raising. Why the present exception?

For the answer one has but to examine the purposes of the current capital campaign. They represent an imperative to finance basic improvements in patient care, teaching, and research. These are the three sides of the historic MGH triangle. No institution can sustain itself without occasional renewals.

With its origins rooted almost in the beginnings of the American republic, the MGH can trace one of its buildings 160 years. More than most hospitals then, the Massachusetts General Hospital has reached a critical point in its physical plant. Massive changes must take place. Only the generosity of friends, though, can make those changes possible.

Unique Nerve Cells May Supply Brain With Vasopressin

(Continued from Page 1)

sin in the spinal fluid samples.

The fact that vasopressin in spinal fluid acts differently from that in blood has led scientists to believe the hormone in CSF originates in its own unique source in the hypothalamus of the brain.

The hypothalamus is a region which governs sleep, temperature, hunger, and thirst, as well as such emotions as fear and anger.

"We used to think that vasopressin was made in only two areas of the hypothalamus," Dr. Reppert said in an interview, "and that subsequently all of the hormone traveled down certain neuroanatomical pathways to the pituitary gland to be stored until needed in the blood.

"We now believe that a distinct population of hypothalamic neurons [nerve cells] produces the same hormone to function within the brain. Within the hypothalamus, a region which acts as a biological clock is one possible site of production of the substance for release into the spinal fluid."

This biological clock is believed to regulate a number of "circadian rhythms" which are attuned to the daily, 24-hour cycle of light and darkness and help to govern such basic aspects of life as sleep and wakefulness.

Studies by a Dutch team of a special strain of rodent called "the Brattleboro rat" provided dramatic evidence of an association between vasopressin and information retention.

Because of a genetic defect, this strain of rat cannot make vasopressin. Under study, the rat demonstrated a marked inability to recall avoidance training. For example, when a normal rat was exposed to an offensive substance, the animal knew enough to avoid contact with the agent in the future. The Brattleboro rat could never remember to stay away.

The investigators corrected the mem-

Photographs: Pages 1, 7, MGH Photo Lab; pp. 3, 4, 8, Myron Daniels; p. 5 (upper), Scott Davis; p. 6, courtesy of Dr. Chiu-an Wang.
Drawing: Page 5 (lower), Edith Tagrin.

ory deficit by administering vasopressin. Injecting it into the CSF proved much more effective than giving the chemical in the blood stream.

Dr. Reppert said that if vasopressin-neutralizing antibodies were injected into the spinal fluid of a normal rodent this treatment would cause a memory defect very similar to that of the Brattleboro subject.

Recently, a team at the University of Oklahoma Health Sciences Center showed that it could induce amnesia in rats by simply disrupting the circadian timekeeping mechanism in their brains.

What the researchers did was create so-called "jet lag" in the animals by radically altering their daily cycles of exposure to light and darkness. The rats could not remember things they were taught shortly before the jet lag started, but interestingly their memory of training given several days earlier did not fade.

Dr. Reppert said he and his coworkers have found highly organized rhythmic concentrations of vasopressin in the CSF of sheep and rhesus monkeys, as well as in cats. He decided to pursue his work with cats, however, because their rhythms are very prominent, thus making these animals excellent models for investigation.

It was also important for the MGH study that the cats be undisturbed and unanesthetized during the slow but painless drawing of spinal fluid because the effects of anesthesia and any stress associated with it might compromise the test results.

Five cats were housed in a special windowless room which enabled the researchers to control times of light and darkness.

Using a metal tube called a cannula, the investigators could continuously withdraw CSF at a constant rate for periods ranging up to 10 days.

Dr. Reppert stressed that at no time were the animals subjected to any discomfort or safety risks.

"Removing the spinal fluid posed no problem whatever for the cats," the doctor declared. "Their bodies replace this fluid much more rapidly than blood. In fact, the spinal fluid is normally turned over several times a day."

The light-dark cycle was rigidly controlled in the experiments. By means of an automated timer the day was divided into 12 hours of light and 12 hours of darkness, except when a special environment was needed.

Dr. Reppert and his associates reported in their article in *Science* that throughout the dark phase of the normal 24-hour day the rhythm exhibited by vasopressin in the CSF indicated low concentrations of the hormone.

Within two to four hours after lights were turned on in the morning, the hormone concentrations increased sharply. Peak values were reached by the sixth to eighth hour of light. By the tenth hour the concentrations began to decline, reaching a minimum shortly after darkness set in.

Robert Coleman, Research Assistant in the Neuroendocrine Laboratory, checks timer to assure a proper cycle of light and darkness during the vasopressin studies.

Although the magnitude of the rhythms varied among the animals, each cat showed consistent peak values daily on an individual basis.

Looking further into this, Dr. Reppert exposed the cats to three days of continuous light. The vasopressin rhythm did not change from the customary daytime pattern.

To determine whether a rhythm from vasopressin could be detected in blood, the investigators obtained plasma from three cats over a 24-hour period. Each cat exhibited a clear rhythm from the hormone in the CSF, but no such reaction could be detected in the blood.

"This finding," Dr. Reppert wrote in *Science*, "suggests that separate populations of neurons are responsible for secreting the peptide into the CSF and into the circulation and that each is regulated by a different control mechanism."

An Assistant Professor of Pediatrics at Harvard Medical School, Dr. Reppert said much more laboratory work remains to be done to understand how vasopressin affects the brain, but he added that it is just possible the hormone may one day demonstrate a potential for improving memory in certain human disorders. ■

Using an automatic pipette, Research Assistant Harley Heath draws a precise quantity of spinal fluid for a test to measure the vasopressin content.

Why Some Patients Call on Doctors

Over-the-counter remedies suffice for most people feeling slightly ill. For others, equally indisposed, only a doctor will do.

(Continued from Page 1)

stomach as a consequence of skipping meals.

Changes in eating or sleeping habits or taking a pain reliever, such as aspirin, turn out most of the time to be just what the doctor ordered, even though he didn't.

Those who do make doctor appointments may not be any sicker than the stay-at-homes.

"If people kept logs on the state of their health, you would not be able to distinguish from the symptoms listed between those who went to the doctor and those who didn't," said Dr. Arthur J. Barsky III, Chief of the Acute Psychiatry Service at the MGH.

Records of individuals seeing doctors in general ambulatory medical practice show 68 to 92 percent of the patients do not have any serious physical disorders.

In fact, in from 10 percent to as many as 60 percent of patients presenting any one of the five most common medical complaints—headaches, chest pains, abdominal pains, labored breathing, and fatigue—no structural disease can be found.

Since many ambulatory medical patients are not seriously ill, Dr. Barsky felt that nonmedical factors could be responsible in large degree for the visits.

Dr. Barsky devoted two years to analyzing the situation. His findings were published in the professional journal, *Annals of Internal Medicine*.

His study of experiences at the MGH and at other centers revealed that stresses of various kinds, psychiatric disorders, social isolation, or informational needs often underlie complaints of physical problems.

Undue concern by a patient over symptoms could alert a physician that something else might also be bothering the person.

"The physician should ask the patient what he imagines is wrong with him," advised Dr. Barsky. "Often the response will initiate a dialogue that will prove most revealing."

The psychiatrist told of a 19-year-old plumber who came to an MGH medical clinic complaining of mild nausea, abdominal cramps, and diarrhea of four days' duration.

A careful history disclosed the symptoms had actually improved after the initial 24 hours. It also turned out that the patient had visited another doctor only a day before coming to the MGH.

Why had he seen two doctors in two days? Why did a common illness that was resolving itself distress him so?

The patient finally explained that some time earlier his mother had suffered what he described as a "burst abdominal tumor" which necessitated emergency surgery. Her illness began with symptoms identical to his and even included a period of improvement.

Rather than concern over his own symptoms, the young plumber was worried about what he thought was causing his sickness. What he really wanted was reassurance that his mother's plight would not befall him.

On numerous occasions an examination will fail to produce any new or changed condition.

A 37-year-old married woman with a long history of multiple sclerosis called for an appointment. The doctor expressed surprise at the visit because the woman's condition, which had not progressed in eight months, remained unchanged, and she had no other medical complaints.

By inquiring "How did you hope I might help you today?," the doctor elicited the real reason for his patient's appointment. Her husband had just been rehospitalized for a recurrent malignancy, she disclosed. She wanted to learn more about his affliction, including his chances for recovery, and felt more comfortable seeking this information from a physician she already knew well.

A doctor visit sometimes reflects a patient's effort to cope with a change in life-style that has proved stressful.

A 63-year-old housewife under treatment for rheumatoid arthritis was always punctual for her clinic dates, but one day she sought a special meeting with the doctor. She spoke vaguely of fatigue. However, her disease did not seem to have gotten worse.

"Have there been any changes in your life recently?" the doctor asked.

The woman thereupon admitted that her senile husband's disability had increased and that she now felt like "a private nurse on duty 24 hours a day."

To help live with the mounting needs of her invalid husband, she thought of taking a brief vacation without him. For peace of mind, she wanted the doctor to endorse her plans as important for her own well-being.

Then, there is the patient who feels the medical care being received is totally inadequate. A check of past medical care experiences may disclose a pattern of consultations with different doctors when faced with life crises or when feeling alone or isolated.

When a physician uncovers a background of "doctor shopping," Dr. Barsky suggests querying the patient as to what the person liked and disliked about previous care givers.

Such questioning proved illuminating in the case of a 59-year-old lonely widow who had made monthly visits to the clinic of a teaching hospital for treatment of insulin-dependent diabetes.

All seemed to go well until her care was transferred from a senior resident to an intern. Control of her diabetes suddenly wavered, and she began arriving late for scheduled appointments.

On questioning by the intern, the woman said she was tired of "being a clinic patient" and of "rotating doctors." She liked the senior resident, she said, because he was "tough" with her, insisting on rigid compliance with appointments and with instructions on taking medication.

"I guess I just need to be told what to do sometimes," she admitted. The more experienced doctor gave her a sense of security, plus a feeling of true interest in her.

By contrast, the intern was less assertive, expecting the patient to undertake greater responsibility for management of her health. The patient felt the intern did not assume sufficient control and therefore did not really care about her.

Dr. Barsky, who is Assistant Professor of Psychiatry at Harvard Medical School, said socially integrated persons can easily obtain advice, interpersonal stimulation, and a sense of belonging from family, friends, and institutions such as churches and clubs, but people who lack such relationships often turn to the physician.

Most patients who visit clinics do not have any serious physical problems.

"People cope with life crises in many ways, and visiting a physician is one such way," Dr. Barsky declared. "In our society it is the doctor who designates that one is sick and should therefore be acknowledged by others as a patient.

"Such acceptance allows a person to relinquish responsibilities and avoid challenges. At the same time, it provides an acceptable means for gaining sympathy, attention, and support."

The psychiatrist emphasized that "hidden reasons" behind some patient visits do not mean their medical complaints are simulated.

"Psychological distress," he said, "causes persons to perceive their health status less favorably; that is, it causes them to amplify, focus on, worry about, and report benign bodily symptoms they might otherwise ignore.

"The general trend of medicine today is back toward primary care. Disease cannot be treated in a vacuum. To be most effective, a physician must be aware of the social setting in which illness occurs and what the psychological repercussions are." ■

Shaped like a butterfly, the thyroid gland straddles the lower, front portion of the windpipe (trachea).

Recognizing Signs of a Faulty Thyroid

The young woman whom the psychiatrist was about to see had a long list of problems.

Her father, who requested the appointment for her, complained in part that his 23-year-old daughter had become so nervous and anxiety-ridden she was no longer manageable.

She had even developed paranoid ideas that unnamed people wanted to kill or attack her. She could not eat or sleep. She lost weight, also her job.

As the MGH psychiatrist spoke with his patient, he noticed her eyes had a prominent stare. Instinctively, he pressed his fingers against the lower part of her windpipe and felt her thyroid gland.

Suspecting that the gland might be functioning abnormally, the psychiatrist sought an examination of his patient in the hospital's Thyroid Unit.

Simple blood tests indeed revealed a hyperactive thyroid. Its production of hormones vital for physical and mental development and, in fact, for the proper functioning of most cellular processes in the body far exceeded normal levels.

Drugs that inhibited the thyroid gland's hormonal production eliminated every one of the symptoms that had made the young woman so miserable.

Not so many years ago when tests for thyroid abnormalities were often crude and nonspecific, as many as 20 to 25 percent of thyroid patients exhibiting mental disturbances were misdiagnosed as having psychiatric illnesses.

Today very sensitive tests, using a technique called a radioimmunoassay,

(Continued on Page 6)

Thyroid Illness Can Have Many Effects

(Continued from Page 5)

assures a precise assessment of a patient's condition, and consequently appropriate treatment.

Involving use of radioactive substances, the tests provide a highly accurate measurement of two thyroid hormones (thyroxine and triiodothyronine) and of thyroid stimulating hormone (TSH), produced by the pituitary gland.

Since TSH secretion is influenced primarily by the level of thyroid activity in the body, doctors can deduce from the TSH output whether the thyroid's production of thyroxine and triiodothyronine is normal. If abnormal, effective care is easily available.

Health statistics indicate that between 4 and 11 million Americans either have or, at some time in their lives, will have a thyroid problem. Hyperthyroidism and hypothyroidism (too little production of thyroid hormone) are equally prevalent in the population.

In addition to symptoms already mentioned, evidence of hyperthyroidism may include heat intolerance, a feeling of pounding in the heart, and bulging, reddened eyes. The latter symptom is characteristic of Graves' disease—the most common form of hyperthyroidism.

Dr. E. Chester Ridgway, Chief of the MGH Thyroid Unit, said that although eye problems often accompany Graves' disease, there is no clear evidence that thyroid malfunctioning causes the eye difficulties.

"We don't know what brings about the proptosis [forward displacement of the eye]," the doctor said. "It just seems to occur with this type of hyperthyroidism. Even when one cures the thyroid disease, the eye condition may need separate attention."

The effect of thyroid activity on the body is so widespread that abnormalities of the gland may express themselves in many ways.

Thyroid hormones, made with iodine from the blood, can stimulate one's heart beat at an extraordinarily rapid rate. With palpitations and a sense of breathlessness, the symptoms can create a picture suggestive of heart failure. In rare cases, this condition does develop.

Severe hyperthyroidism may also cause extreme muscular weakness in the shoulders, arms, and upper portions of the legs. The patient may no longer be able to climb stairs or raise the arms to put things on shelves.

Several forms of treatment are available for an overactive thyroid. Antithyroid drugs can be given to reduce the gland's hormone-making ability, or the doctor may suggest using radioactive iodine, which localizes only in the thyroid gland. This special iodine preparation tends to decrease the size of the thyroid tissue.

The MGH and Massachusetts Institute of Technology, working together, helped usher in the era of nuclear medicine when in 1939 they pioneered the use of radioactive iodine for thyroid problems.

Surgical removal of some of the gland

Patient with enlarged thyroid gland has Hashimoto's thyroiditis, a common form of hypothyroidism in the United States.

to reduce function to a normal level is also an option. This is especially delicate work because of the proximity of other important structures, such as the vocal cords.

Some studies are under way to determine whether psychological stress can lead to hyperthyroidism. A number of investigators believe such stress can affect the thyroid by having an impact on the region of the brain which controls the gland.

In hypothyroidism, as in its counterpart, the predominant symptom may appear to be psychological, such as depression. Other indicators include cold intolerance, dry and sometimes thickened skin, a hoarse voice, constipation, a gain in weight, tiredness, and general apathy.

An MGH physician related that several years ago he traveled home on vacation and found his father ill. "He had been diagnosed as having Parkinson's disease [a neurological disorder marked by muscular rigidity and tremor]," the doctor said, "but he was also treated for depression because he appeared very lethargic. Everyone thought this was due to the Parkinson's."

Because other symptoms which could be associated with hypothyroidism also were present, the doctor drew a sample of his father's blood and had it tested on return to the MGH. "He was extremely hypothyroid," the physician remarked. "Treatment with thyroid hormone eliminated most of the symptoms linked to the glandular problem, including the apparent depression."

A strong clue to the presence of the hypothyroidism was a family history of the disease. The doctor said his sister, an aunt, and an uncle also had suffered earlier from the illness.

Dr. Ridgway, who is Associate Professor of Medicine at Harvard Medical School, said two main conditions account for hypothyroidism in the United States.

One condition is called Hashimoto's thyroiditis. Antibodies in the blood and certain white blood cells (lymphocytes) attack and destroy the thyroid tissue. The disease, which in the early stages usually includes a glandular growth (goiter), commonly runs in families and is most often seen in women.

"The best marker for this illness," Dr. Ridgway said, "is an acceleration in the secretion of TSH by the pituitary gland. The combination of a low thyroxine and a high output of thyroid stimulating hormone makes the diagnosis."

Nearly half the incidence of hypothyroidism in this country can be attributed to Hashimoto's thyroiditis. Most other patients with an underactive thyroid gland are people who at one time were treated for hyperthyroidism.

Unlike the effects of an overactive thyroid gland, hypothyroidism can slow the heart and cause a dilatation of the heart.

All muscles in the hypothyroid patient become weak, and painful muscle cramps may occur.

The patient's respiration may decline dangerously because thyroid hormone deficiency makes brain receptors less sensitive to the gases which control breathing. Carbon dioxide in the blood

Community Service Ranks High at MGH

(Continued from Page 1)

oldest in the nation would be marked by almost constant change. The steady growth alone of Boston's population, then about 25,000 inhabitants, was bound to produce ever increasing demands for medical care.

By 1847, extensions had been added to both the East and West Wings of the Bulfinch Building, almost doubling its patient capacity. In 1973 the structure became a registered National Historic Landmark.

Today, 160 years after the MGH first opened its doors, some 17 buildings dot the hospital landscape which now spreads over 13 acres. The institution has served more than 1,451,000 inpatients.

The bed capacity has grown from an initial 73 to 1,092. The annual admission rate of 115 patients in 1822 has soared to some 30,000.

Another half million people each year visit ambulatory units or the offices of private doctors at the MGH for outpatient care. In the past, many of the illnesses so treated would have required hospitalization.

Despite its phenomenal growth, the hospital's commitment of service to the community remains a deeply rooted one. Eighty percent of patients who enter the MGH live within 40 miles of Boston.

The remainder converge on the hospital from throughout the world, most of them referred by doctors because of the special expertise and technology available here to deal with complex afflictions.

An illustrious physician of early days at the MGH, Dr. Oliver Wendell Holmes, once described how Dr. James Jackson, a cofounder of the institution, viewed his role in medicine.

Dr. Holmes said Dr. Jackson considered it his duty as a physician "to lean with his whole weight on the side of life and shift the balance in its favor if it lay in human power to do it."

The worldwide reputation that the MGH has built clearly demonstrates that Dr. Jackson had plenty of company in the judicious adaptation of that self-imposed mandate.

As with everyone else, however, the power of doctors has limits.

Last February, in an address to several hundred friends and staff members, Dr. Charles A. Sanders, then MGH General Director, remarked:

"The MGH has achieved many things in patient care, research, and education. However, as the patient care and research buildings have grown older and older, our health professionals increasingly have had to work harder to maintain the standards we cherish for our patients.

"To meet the challenges of tomorrow, we need to make some sweeping physical changes to replace facilities that will soon become obsolete."

John E. Lawrence, President of the Massachusetts General Hospital Corporation, said the institution's "internationally known professionals work their miracles in spite of, not because of, the physical plant."

The gathering marked the kickoff of a campaign to raise $114 million so that

The Baker Building, opened a half century ago, will cease to house patients when new quarters become available.

the hospital can continue to advance the frontiers of medical knowledge.

Pledges totaling more than $30 million, including what is believed to be the largest single gift ever made to any existing American hospital, propelled from the starting line the biggest drive in the history of New England hospitals.

Arthur O. and Gullan M. Wellman of Florida provided the major thrust by committing $15 million to build and equip a new research facility to be known as the Wellman Research Building.

Space for the structure will be created by widening the present Edwards Research Building, constructed in 1951, and extending it to join another MGH building, Bartlett Hall.

A few years ago, Mr. Wellman, a member of the MGH Corporation, and his wife financed establishment of the Wellman Research Laboratories in the hospital's Department of Dermatology. Part of the new contribution will provide ongoing support for operating expenses of the laboratories where studies on the use of light in treating certain diseases are conducted.

The new Wellman Research Building will enable investigators of varied specialties but mutual interests to work more closely together. Broad in scope, the programs to be undertaken will embrace such areas as aging, nutrition, the neurosciences, endocrinology, metabo-

(Concluded on Page 8)

---

builds up. Unchecked, the condition can lead to CO_2 narcosis, coma, and death.

Each year in the United States, about one of every 5,000 newborns is found to have hypothyroidism (*MGH News,* March 1978). Mental and physical development normally progress at a very rapid rate at the time of birth. If such processes are slowed by lack of thyroid hormone, some of the deficits can never be made up.

Many states, including those in New England, routinely screen all newborns for this condition, known in its worst form as cretinism.

The malady can be found in a number of underdeveloped countries where diets lack iodine needed by the thyroid. Such iodine deficiency is not seen in this country.

Hypothyroidism is described as among the easiest diseases to treat. Needed hormone can be administered simply and safely.

Dr. Ridgway emphasized that awareness of a family history of thyroid trouble is extremely valuable for early detection of such problems.

"Our country has an enormous population with thyroid disease," he pointed out. "Since both hyperthyroidism and hypothyroidism often run in families, knowledge of such a background is as important for proper thyroid care as is a family history of coronary artery disease or hypertension in helping to guard against those conditions." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Modern Care Requires More Space

(Concluded from Page 7)

lism, skin diseases, and growth and development.

Some $80 million of the funds being raised will be used to renovate areas or replace more than 500 beds in sections of the hospital which have become cramped and outmoded.

The plans include a new building to replace beds now in the Baker Building, the semiprivate pavilion; all beds in the Vincent-Burnham Building, which contains the Gynecological Service and the Children's Service; and certain beds from the Phillips House, the private pavilion, and from the White Building.

Inpatient care planning also calls for renovations to provide for surgical beds, relocation of some existing beds to new patient rooms, a moving of the Burn Unit, and transfer of all remaining patients in the Bulfinch Building to other quarters.

None of the changes on the drawing boards will increase the hospital's present bed capacity.

New rooms for patients will be larger, and corridors will be wider to permit efficient transport of advanced technological equipment of many types and to improve patient comfort.

"Raising the $80 million or so will be our biggest challenge," said Dr. Joseph B. Martin, Interim General Director. "We need those inpatient beds very much."

Dr. Martin believes that a windfall $50 million-plus research agreement with Hoechst AG, an international chemical firm, may inadvertently slow the $114 million drive.

"Many potential donors may have adopted the attitude, 'With all that Hoechst money, the MGH now has all it needs,' " Dr. Martin said. "Not so. We can't use one cent of that toward the $114 million. Even the annual fund drive returns go for other requirements.

"We do have about $38 million of the $114 million. However, we still have a long, long way to go. And only a small percentage of that nearly $38 million given so far is for replacing the patient care beds."

From campaign funds a total of $5.2 million will complete financing of the $32 million Ambulatory Care Center, which is nearly operational.

Replacing a structure which was constructed in 1903 to handle 300 patients a day but manages to serve 1,400 daily, the nine-level center will be able to accommodate 600,000 ambulatory patients annually once it is fully opened.

It will house most of the services now found in the old Clinics Building as well as physicians' offices, ambulatory surgical and radiology suites, a satellite pharmacy, some specialized laboratories, and appropriate administrative services.

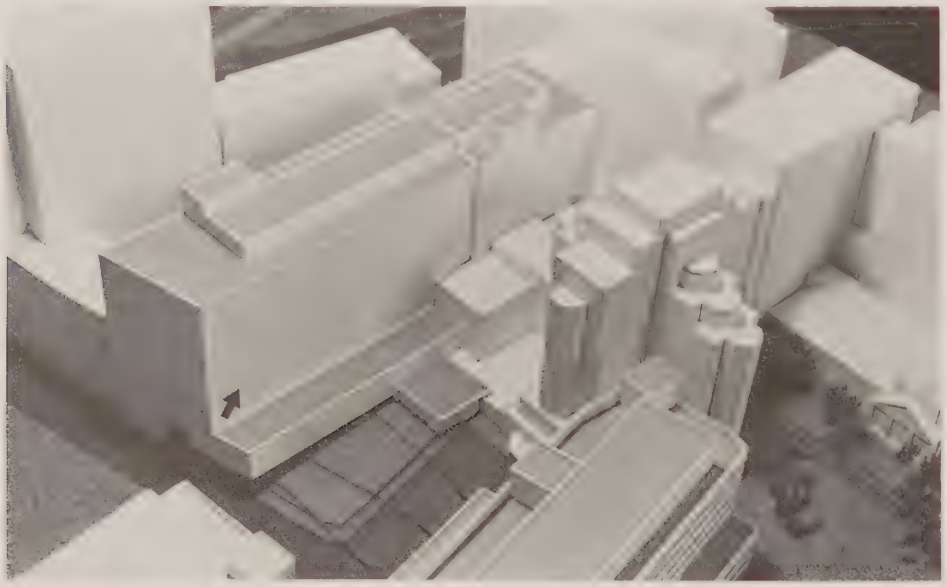
The Cox Center, which treats 18,000 cancer patients a year, needs another $2 million to fulfill remaining obligations on that building which opened in 1977. Three floors are used for the diagnosis and care of ambulatory cancer patients while other floors are devoted to research.

The MGH hopes to allocate $10 million to its year-old Institute of Health Professions. In addition to its initial programs offering a master's degree in physical therapy and a certificate of advanced study in social work, the Institute this fall launched a master's degree program in dietetics for registered dietitians.

Funds earmarked for the Institute will permit endowment for faculty support and for scholarship aid, assuring a broad mix of students.

The Treadwell Medical Library, serving both physicians and lay employees at the MGH, looks forward to $2 million in improvements, including conversion of important materials to microfilm. The hospital also plans to combine with Treadwell the Palmer-Davis Nursing Library, situated in Ruth Sleeper Hall.

The physical ills that the passing years inflict call for rigorous attention. Only by keeping its own state of health in top form can the MGH continue to advance the frontiers of medical knowledge through patient care, education, and research. ■



The long rectangular structure (see arrow) to the left of the MGH's main entrance represents an alternative proposal for situating new inpatient care facilities.

MGH News

Vol. 40 No. 9 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS December, 1981

Curing the Emotional Ills of Very Young Children

The Effect of Burns Underlines the Need To Practice Caution

The child lay motionless to avoid increasing the pain of the burns that covered much of his body. Surrounding his bed, a plastic curtain protected his wounds from possible bacteria.

Clipped to the foot of the bed hung the young patient's medical record, and something else—his photograph, taken before the accident which had engulfed him in flames.

Parents regularly volunteer these photos to help guide plastic surgeons in rebuilding the distorted features of patients.

Not just one but three of the four special Bacteria Controlled Nursing Units at the Shriners Burns Institute bore photographs. Two of the patients were teen-agers injured in an October explosion and fire which shattered an aerosol plant in Holbrook, Mass. Twenty-four people were hurt, three fatally.

"A burn destroying the full thickness of the skin over a wide area of the body is the worst injury that a person can suffer," said Dr. John D. Crawford, head of the Endocrine-Metabolic Unit in the MGH Children's Service and Chief of Pediatrics at Shriners, an MGH affiliate.

"If a person suffered a heart attack or stroke, or were hit by a truck, a physician generally could tell the patient's family in a week or 10 days whether the crisis had passed. But for severely burned children here at

(Continued on Page 4)

In the past, if a young child had psychological problems, they were generally not detected until the youngster entered school. At that time, teachers could measure a child's actions against those of peers, spot any significant deviations in behavior, and call the attention of parents to a need for professional help.

Today, many mental health professionals feel it is important not to wait until a child reaches kindergarten before investigating emotional difficulties.

In an effort to nip childhood problems when they develop instead of later, care givers are focusing on the younger age group, ranging from infancy to five years.

Resentment for some reason is clearly etched in the face of this tot.

The MGH Child Psychiatry Service began devoting increased attention to these children 18 months ago as a new and vitally needed dimension in the hospital's care of the young.

"These are children whose entire emotional development has revolved around relationships with parents and siblings within the home," said Dr. Muriel Sugarman, an MGH child psychiatrist.

"The children are at an age when the course of their life is most flexible. If there are problems, a child usually can be put on the path of normal development in very little time and for very little money."

"Failure to thrive" ranks high on the list of conditions affecting disturbed children. The reason for slow growth and weight gain could be medical, but it could also stem from the manner in which parents interact with their children.

Dr. Sugarman told of an 8-month-old girl whose feeding had been consistently difficult since a very early age. After the baby was hospitalized for failure to thrive, doctors learned that, rather than resist her daughter's reluctance to eat, the mother had deliberately skipped the child's mealtimes. When the father came home from work, he fed her.

An investigation disclosed that a number of factors contributed to the child's difficulties. The mother was handicapped, had little support in the home, felt inadequate to raise the daughter, and did not want to become pregnant in the first place.

Professional counseling helped to change the mother's attitude. She was

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, MA. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
Joseph B. Martin, MD, *Interim General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIAL:

You And Your Tennis Elbow

You can develop it from using a screwdriver. Or even a hair dryer. But the condition is called tennis elbow. In any case it hurts when you do things like use a screwdriver. Or play tennis. Often the elbow will ache for weeks or months. Like many similar joint disorders described in a page 7 article, tennis elbow pain that comes right after an activity is helped by ice, not warmth. The joint also needs rest from stressful activities.

Once the elbow starts feeling better, exercise helps insulate against recurrence. For example, while seated, hold a five-pound weight in the appropriate hand, palm up, wrist supported by your knee. Curl the wrist up slowly and hold for three to six seconds. Start with five repetitions. Build up the number over a period of time until you can comfortably do 25 two or three times a day. Should your pain be in the inside of your elbow carry out the same exercise with your palm down.

Your shoulder muscles also need building up to prevent a recurrence of tennis elbow. First slowly raise a five-pound weight five times straight in front of you to shoulder height with arm outstretched. Then lift the same weight five times sideways to shoulder height.

If you do play with a not too severe tennis elbow, prematch precautions make sense. Massage your elbow before playing. Before you hit, some forearm isometrics and upper-body stretching will help. You should both stretch and use isometrics on your wrist, forearm, and shoulder. As you begin to rally, hit lightly for 15 minutes. Using a two-inch wide commercially available forearm support band just below the elbow and perhaps a second one just above the wrist may also help. Be careful not to make the support fabric too tight. Then enjoy. Sensibly.

Painful But Preventable

Burns are the most traumatic of all injuries. They are also preventable. Take the time to read the page 1 article on preventing burns.

Explaining a Child's Emotional Behavior Can Be Difficult

(Continued from Page 1)

also advised that feedings would progress more smoothly if she frequently offered her daughter food that she enjoyed eating and could hold herself, such as pieces of fruit.

In another situation, an infant boy not yet 9 weeks old vomited excessively. Initially, surgeons widened the outlet from his stomach into the small intestine.

After undergoing a second procedure, the boy had an uncomfortable sense of fullness. He became a feeding problem and at 7 months of age was brought for the first time to the MGH. The reason: failure to thrive.

"A surgeon inserted a tube into his stomach so that if he refused to eat by mouth, he could be fed through the tube," Dr. Sugarman said. "Once the pressure was off the mother to get food into him by mouth, he began to eat more on his own. As he gained weight, the mother became less anxious, and the tube less necessary."

Although most inpatient troubles center on feeding, some youngsters are evaluated for inability to speak.

Dr. Sugarman recalled a 2-year-old boy who had a good relationship with his family but nevertheless became easily frustrated and screamed if something did not go just right. At his age, he should have developed a 50-word vocabulary and a capability of formulating two- or three-word sentences, but he had not yet achieved this plateau.

Dr. Sugarman obtained a detailed history of the child's development while an MGH child psychologist, Kristen J. Kuehnle, who holds a doctorate in education, administered tests to determine if any developmental disorder existed.

The studies revealed that in addition

Photographs: Pages 1, 3 (lower), courtesy of Massachusetts Society for the Prevention of Cruelty to Children; pp. 3 (upper), 5 (upper), 6, 8, Myron Daniels.

Drawings: Pages 4, 5 (lower), courtesy of Project Burn Prevention; p. 7, Robert Galla.

In the arms of his mother, this 1-year old seems not to have a care in the world.

to suffering from a seizure malady (epilepsy), which the parents already knew about, their son had a hearing impairment and a learning disability of which they were unaware. The latter conditions accounted in the main for the boy's poor control over his behavior and his delayed speech.

In the ambulatory clinic of the Child Psychiatry Service, staff members frequently see 2- or 3-year olds who constantly disobey and are destructive without apparent reason.

"In an effort to sort out what is wrong, we have to go back, almost to the time of the child's birth," Dr. Kuehnle said. "We ask the parents whether their son or daughter had been difficult from the beginning. The root of the problem could be an unrecognized brain injury, such as one from insufficient oxygen during delivery.

"Perhaps the child was fine until 18 months or 2 years and then started to say 'no' to everything. If unable to cope, the parents might give in to the youngster's every desire. Or, at the other extreme, they might become angry and spank him. In either situation, an all-or-nothing response."

The parents need to understand what is going on in the child's mind. The arrival of a new baby in the family, for example, could indicate to a 2- to 4-year old that he was not good enough or loved enough. So from anger he misbehaves. Instead of punishment, the child needs reassurance and calm limit-setting.

Dr. Sugarman, an Instructor in Psychiatry at Harvard Medical School, cautioned that when parents accede too much to their children's whims, the youngsters may soon begin to make totally unrealistic demands. At this point, the parents must shift gears and perhaps even take away some privileges.

Sometimes in the ambulatory clinic parents complain that their youngsters are hyperactive only to discover that their own upbringing had been so restricted they are unable to recognize and tolerate a child's normal range of activities.

Some children who *are* hyperactive are deeply upset inside. Often spanked for minor infractions, such a child is both afraid of punishment and filled with anger. In emotional turmoil, he becomes negative to everything, throws toys around, jumps from one activity to another, cannot settle down, and cannot concentrate.

On occasion, hyperactivity has a neurological basis. "In these youngsters, the nervous system is just firing off all the time," Dr. Sugarman declared. "The children are not reacting to any outside influence. This group often is not detected until school age."

Although specialists look for psychological ills in children at the earliest possible age, attendance in school can be extremely important in sizing up a child's mental attitude.

Out of the home where they might have gotten their way all the time, the children now find themselves under different supervision and in an environment where they must share things and obey rules.

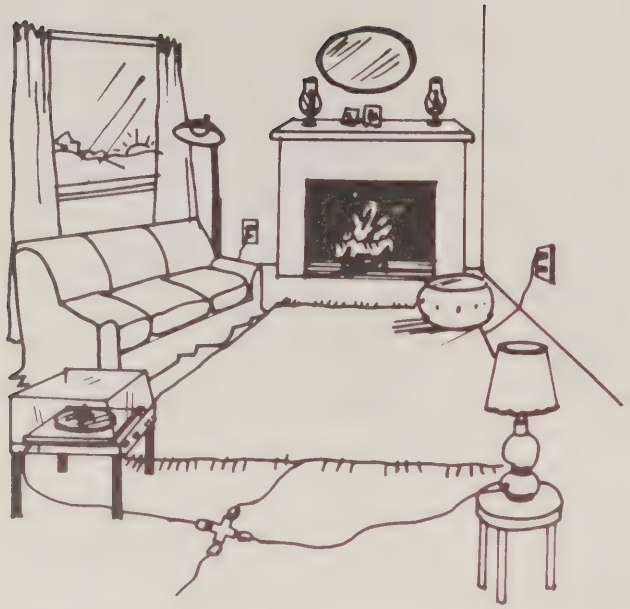
Does a particular child relate well with others? How well does he concentrate when he draws? Does he tend to smash toys? Does he become upset if things get dirty? At an age when he can verbalize, testing becomes easier.

Research studies indicate, however, that even infants can communicate, albeit not by speech. Mothers can usually sense the meaning of a baby's cry, movement, or facial expression.

Investigators have suggested that if one person took care of an infant and learned and responded to the baby's signals, the child would cry less, sleep more regularly, eat better and in general be more predictable.

"As research on infancy increases our knowledge of early development, it will be possible to intervene earlier to prevent some of the lifelong consequences of emotional disorders in very young children," Dr. Sugarman said. ■

When a parent's attention is focused on a younger child, a 2- to 4-year old can sometimes get the impression of not being loved as much.



Fire hazards in this living room include an electrical cord running under the rug, a power overload, and lack of a fireplace screen.

Types of Burns Correlate With Age

(Continued from Page 1)

Shriners it might take not 10 days but 100 days—more than three months—before we could say, 'He is going to make it.' "

And while they can achieve much more than before, plastic surgeons can do only so much. Bad burns leave scars, both physical and emotional, reminding the victim of the tragic episode he underwent. Despite the help of photos, no plastic surgeon can restore the original appearance.

For the past several years, Dr. Crawford has served as Principal Investigator of Project Burn Prevention, a federally supported program which has embraced the MGH, Shriners, the Education Development Center in Cambridge, Mass., and the National Fire Protection Association.

Together, these centers have studied how, where, and to whom burn injuries most often occur and what might be done to minimize the danger.

Dr. Crawford said that when a referring physician calls the burns institute and says he wants help for a 2-year old, doctors at the center can make a pretty accurate guess as to the nature of the injury.

"For a child around the age of 2, the odds are better than 9 out of 10 that hot liquid was involved," Dr. Crawford said. "Children at that age pull at everything they can. If it's a tablecloth, a cup filled with hot coffee could come tumbling down. If the child is a little older and can reach to the top of a stove, a pot handle extending over the side might prove an attractive target for grabbing."

He also cautioned that youngsters of 2 and under put everything into the mouth, and there is nothing more dangerous than an electric cord that is still connected to an outlet.

When an electric iron is hot enough, for example, the mother often unplugs the cord from the appliance. A baby or toddler could take the plug into the mouth and suck on it. The child's saliva, acting as a perfect conductor of electricity, would ensure a particularly disfiguring burn.

Although several feet from the lawn mower, the pilot light of the water heater can easily ignite gasoline vapors escaping from the mower's tank.

"Laws should be passed that the plug into any electrical appliance should be a permanent connection," Dr. Crawford emphasized. "The only unplugging should be done at the wall outlet. And even if unplugged from the outlet, cords to such appliances as irons, coffee pots, and hot crocks should never be left dangling."

At around 5, 6, and 7, children go through an imitative phase, deriving fascination from forbidden acts, such as lighting matches.

So as not to be caught, the children play with the matches where they will not be seen, in closets and bedrooms.

"I submit that every child of that age should be taught how to use matches," Dr. Crawford declared. "A positive approach rather than a rigid ban would make playing with matches less dangerous and less of a temptation."

The burn victim in the 12-to-15-year-old range generally is someone who, while out with his buddies, offered to demonstrate his courage, perhaps in response to a challenge.

Such bravado causes many motor vehicle accidents. One person in every five killed in a highway crash succumbs from burns.

High tension towers also attract the young daredevil, who is ignorant of the hazards of high voltage electricity. Goaded by his pals, he climbs a tower, risking contact with wires that could inflict a burn sufficient to cost him his limbs or his life.

Dr. Crawford commented that accidents of this kind almost never happen with only the victim present.

Teen-agers enjoy adjusting or repairing bicycles or motorcycles, and to clean up the resulting mess in a garage or cellar, they frequently turn to gasoline.

"A tiny pilot light in a nearby heater could come in contact with fumes from the gasoline and trigger a tremendous explosion," the doctor warned. "The gasoline itself doesn't have to be near the flame."

As part of their work toward burn prevention, Dr. Crawford and his colleagues have devised special high school courses on how electricity and gasoline behave.

What about teen-aged girls? In learning to cook, they suffer some burn injuries resulting from carelessness. But more important, they dress up for parties, and the more frilly, loose-fitting the clothes are, the more flammable they are. Parties connote candles and

Aspirin: More Potent Than Many Think

It is a potent drug with many uses. It helps in treating menstrual cramps, arthritis, nerve pain, fever, headache, and aching muscles.

This same drug fights blood clots. It may prove useful in preventing heart attacks and strokes.

Although it has many side effects, you can obtain it over the counter.

Its name is aspirin.

The popular remedy or close cousins of it have benefited mankind since ancient days.

Over the centuries aspirin has developed into such a universal medication that today, whenever they feel out of sorts, most people reach for it, often without confirming the real nature of their problem.

Continuing research into aspirin, more formally known as acetylsalicylic acid, has produced exciting new possible uses for the drug but also a greater awareness that for some patients who take it important cautions are in order.

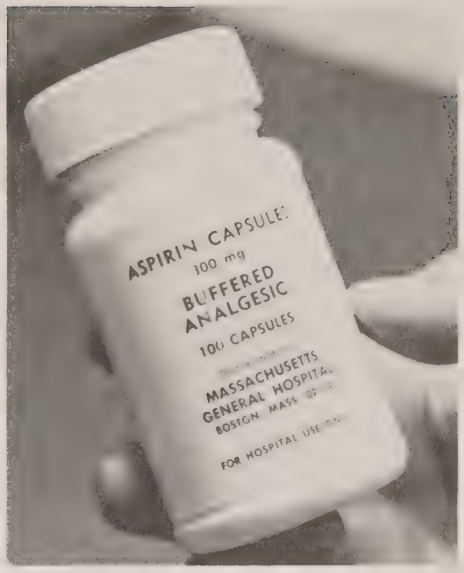
Numerous studies are under way to determine whether, in addition to other benefits, aspirin can help ward off heart attacks and strokes caused by clots in blood vessels.

In this regard, investigators seek to take advantage of one of the drug's major side effects: its ability to cause bleeding.

Aspirin has demonstrated that it can interfere with the clot-making machinery in blood by slowing the formation of certain natural body substances called prostaglandins.

Cells throughout the body produce them. Some 50 types have been identified, but physicians still have much to learn about these hormone-like agents.

In affecting blood, aspirin acts to block the formation of two types of prostaglandins. One, called *thromboxane,* is secreted by platelets, the chief clotting factor in blood. The second, called *prostacyclin,* is made by cells in the walls of blood vessels.



Formulated by the MGH, this highly buffered aspirin is used by many arthritis patients.

Thromboxane stimulates platelets to gather, thus promoting the development of clots, and is the most potent constrictor of blood vessels known. By

(Continued on Page 6)

open fires.

Beyond the teen-age years, carelessness at the work bench, both on the job and at home, accounts for many burn injuries treated at the MGH Burn Unit. In the winter, many motorists seek treatment for face, hand, and eye burns caused by overheated radiators and eruptions of battery acid.

Most fatal burns, however, occur in house fires, and a large proportion of such blazes are traced to people who were smoking while tired or under the influence of alcohol.

Burn statistics are staggering. Two million Americans suffer serious burns each year. More than 70,000 require hospitalization, and 9,000, a third of them under the age of 15, die from their injuries.

Some bright spots, however, dot the otherwise bleak picture. For example, in 1976 when the government banned Tris, a flame retardant fabric used in sleepwear, as a possible cause of cancer, health and safety officials feared a resurgence of sleepwear burn injuries. But no such outbreak occurred. Through modification of design, weave, fiber, and treatment, manufacturers developed other flame-resistant night clothing.

In Dr. Crawford's view, the advent of the smoke detector may cause the biggest reduction in fire deaths since the early 1900s when electric lighting replaced the gas light.

"More and more communities are recognizing the importance of smoke detectors in buildings and are passing ordinances requiring their installation," he said. "In 1975, fewer than five percent of homes had a smoke detector. Today, 60 percent of households have them."

The National Fire Protection Association describes the detectors as a family's first line of defense against a fire (*MGH News,* January-February, 1981). What is more, the devices are inexpensive—many sell for under $10.

And to medical investigators like Dr. Crawford, who is also Professor of Pediatrics at Harvard Medical School, the study of burns provides hope for the future.

"Unlike accidents which are totally unpredictable, having no rhyme or reason, burns often correlate with such factors as age and sex," the doctor said. "We call that epidemiology. When you have epidemiology, prevention is possible." ■

With her sleeve on fire, this woman could step quickly to a sink and run water onto the flames. But if the front of her dress had ignited, her best move would be to roll on the floor to smother the blaze.

Aspirin's Effect on Blood Raises Hopes

(Continued from Page 5)

blocking the action of an enzyme necessary to make thromboxane, aspirin in effect prevents the clot.

Too large a dosage of aspirin, however, can have a reverse effect by stemming the output of prostacyclin. This prostaglandin's natural function is to inhibit clotting by preventing platelet aggregation and by keeping blood vessels dilated.

"Where do we strike a balance?" asked Dr. Carl E. Rosow, an MGH anesthetist who also holds a doctorate in pharmacology. "At what point can we say that such and such a dosage will fight clotting and not interfere with the body's own anticlotting mechanism? The answer to this crucial question is not in yet."

Although the optimal dosage is unknown, many physicians nevertheless recommend minimal daily amounts of aspirin for patients considered at risk for heart attack or stroke.

Similarly, small dosages are prescribed for those kidney dialysis patients who tend to develop clots in shunt tubes carrying their blood to machines which filter out impurities.

And some surgeons recommend aspirin for men undergoing total hip joint replacements. Blood clots commonly occur after this type of operation because the procedure involves dislocating the hip. This leads to a twisting of veins, making the vessel walls susceptible to injury.

For some unknown reason, women having a hip joint replacement do not exhibit the same anticlotting protection from aspirin that men do. Researchers are trying to explain this paradox.

Doctors feel the quantity of aspirin they prescribe is too small to cause harm and in the long run may prove to do a lot of good.

"The average person doesn't fully appreciate aspirin's efficacy," said Dr. Rosow. "It's extremely effective in the treatment of many conditions. Studies have shown that for certain kinds of pain, usually involving a large inflammatory component, aspirin is better than some of the oral narcotics."

Aspirin has long stood as the treatment of choice for the painful inflammation of rheumatoid arthritis (*MGH News,* January-February 1978).

In some individuals, however, plain aspirin tends to irritate the lining of the stomach. Under such conditions, chronic, heavy use of the drug could lead to serious gastrointestinal bleeding and ulcers.

To reduce the possibility of such side effects, a number of pharmaceutical firms market aspirin containing a buffering agent to counter stomach acidity.

"The problem with this is that the amount of buffer put into each tablet is inconsequential," Dr. Rosow said. "The only aspirin product available that really does provide a significant amount of buffer is the effervescent type. Not only is it highly buffered, but when taken it is already in solution."

But even the effervescent product has an objectionable feature. Its high sodium content makes it unsuitable for individuals on low-salt diets and for daily, long-term administration.

Still another type of aspirin being marketed is the enteric-coated or, so-called, time-delayed pill. Coated with a preparation resistant to the action of stomach acid, this tablet does not dissolve until it reaches the small intestine. Several studies indicate enteric-coated aspirin causes less gastrointestinal bleeding than either the plain or buffered type.

Since the time delay means a slower breakdown of the tablet, however, its pain-relieving and anti-inflammatory effects are somewhat held up.

As might be expected, both buffered and enteric-coated aspirins are more costly than the plain ones.

Inevitably, the question arises, "Should I buy expensive brand-name aspirin or the much cheaper aspirin products carrying little advertised, store labels?" Aspirin, after all, is aspirin.

"It all depends on the intended use," Dr. Rosow said. "The costlier aspirin is probably made a little better. Fewer broken pieces are found at the bottom of the bottle, and there's less chance of a vinegary smell, signaling decomposition.

"But if the intent is to relieve a simple headache, the less expensive product will probably do the job just as well."

In contrast, he added, consider the patient taking 18 or 20 aspirins a day for rheumatoid arthritis.

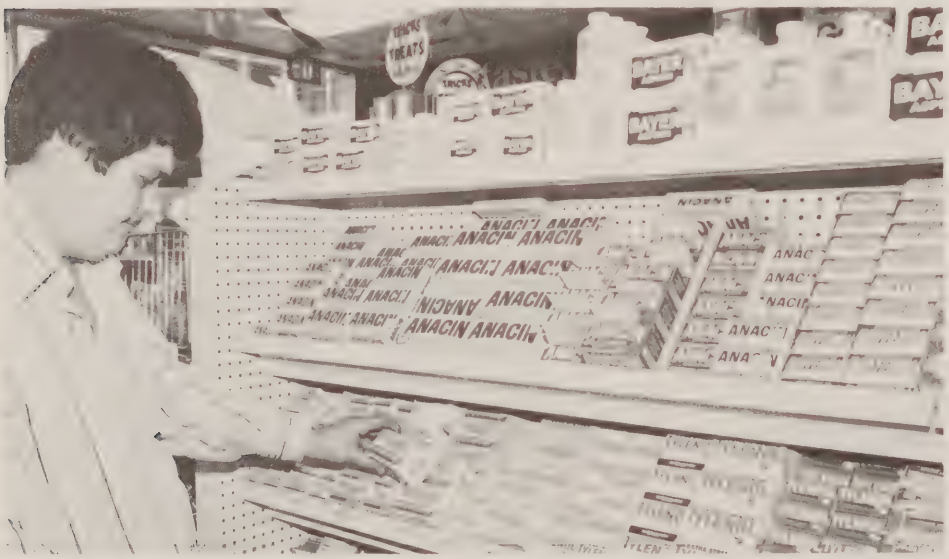
"Such individuals must have an aspirin dose that is dependable and repeatable from bottle to bottle," he said, "because the amount of aspirin they take is practically at the point of toxicity."

Dr. Rosow said that unfortunately because these patients must take so many aspirins, they usually are the ones who first feel the cost pinch and turn to the lesser known labels.

Some types of aspirin are labeled "extra strength" but simply contain more of that drug than the customary 325 milligram (5 grain) dose per tablet.

Other products boast a combination of aspirin and other nonnarcotic pain killers (analgesics). Most trials indicate that these combinations offer no more pain relief than an equal-sized quantity of aspirin alone.

For people who cannot ingest any form of aspirin because they have bleeding tendencies, stomach problems, or gout or because they are taking anticoagulant or antidiabetic drugs,



People seeking a pain reliever can choose from many brands of over-the-counter aspirin and nonaspirin products.

What Seems Like Bursitis Might Be Tendonitis Instead

Many people insist on being creatures of habit, even if it hurts.

How often have you heard, "Every time I put my coat on, my shoulder aches." People fail to realize how easily they can irritate the shoulder, yet how simple the remedy often can be.

On donning a coat, for example, if the right arm goes into a sleeve first, the other arm must be pressed backward and twisted to catch the inner opening of the other sleeve. Such motion would aggravate any painful condition in the left shoulder.

If the individual reversed the pattern and put the left arm into a sleeve first, he could avoid stressing the ailing shoulder. People, however, become so set in their ways they find it difficult to alter even this simple maneuver.

Ask someone with a painful shoulder what the problem is, and the reply probably will be, "I've got bursitis." Chances are it is not.

Dr. Hugh P. Chandler, an MGH orthopedic surgeon, says that patients who come to his office seeking relief from shoulder bursitis usually turn out to have tendonitis.

Bursitis means inflammation of a bursa, a closed sac containing a lubricating fluid. Bursae are found over bony prominences near joints. The sacs, acting like cushions, enable tendons and muscles to glide over the projections.

Although most often affecting a shoulder, bursitis may also occur in an elbow, hip, knee, or foot, producing swelling, inflammation, and pain. Repetitive irritation, a banging, or infection are the primary causes.

In the shoulder, the bursa most susceptible to injury sits atop the upper arm bone (humerus). Just above is an arch formed by a corner of the shoulder bone (scapula) and an end of the collar bone (clavicle).

Shoulder bursitis usually stems from an inflammation of a sac, or bursa, situated atop the upper arm bone.

Three major muscles weave through that arch and during movement of the shoulder can become "nutcrackered" between the bones. The inflammation that results is tendonitis.

"A physician examining a patient with tendonitis in the shoulder can usually move the individual's arm gently without inflicting any pain," Dr. Chandler said. "But if the patient moved his arm with the physician placing resistance against it, there would be considerable discomfort.

"If the patient had bursitis, movement of the arm more than a few degrees in any direction, even without resistance, would be very painful.

"In short, with tendonitis, you hurt some of the time; with bursitis, you hurt all of the time."

With tendonitis, the patient can wait several weeks for a medical appointment. The person with bursitis usually wastes no time getting to a hospital emergency room.

Treatment of bursitis involves inserting a needle into the bursa and withdrawing (aspirating) its fluid, which is much like the lubricating fluid within a joint. Then the doctor injects an anesthetic, procaine hydrochloride (Novocain), and cortisone (an anti-inflammatory agent) into the emptied sac.

"The results are usually dramatic," said Dr. Chandler, who is also Assistant Clinical Professor of Orthopaedics at Harvard Medical School. "In just 24 hours the patient is much better. Often, the bursitis patient will not have another attack. Tendonitis, on the other hand, frequently recurs."

In treating tendonitis, Dr. Chandler avoids using a needle because he says the tendon might weaken and rupture. Instead, he advocates the use of oral anti-inflammatory drugs and avoidance of positions that impinge upon the tendons.

With regard to an ailing shoulder, these positions could include reaching for something on a high shelf or, while sitting behind the wheel of a car, straining to get an article from the back seat.

If tendonitis has been present for a long time, calcium will sometimes form in the tendons and spread into the nearby bursa, causing calculus bursitis. Usually, before aspirating a bursa, the doctor will order an X ray to determine the presence of any calcification. Such deposits can be treated with drug injections.

Bursitis and tendonitis can lead to complete immobility of a shoulder. Recovery from a "frozen shoulder" is a slow process involving corticosteroid injections over a period of months to counter inflammation. Later, to regain full range of motion, the patient will undergo exercises closely supervised by a physical therapist. The treatments may take as long as 18 months.

Next to problems in the shoulder,

(Concluded on Page 8)

there is an alternative.

Aspirin's growingly popular competitor is called acetaminophen. It is marketed under many brand names.

Acetaminophen relieves fever and common aches and pains with an effectiveness comparable to aspirin but does not irritate the stomach. Unlike aspirin, acetaminophen lacks the ability to reduce inflammation in sore muscles or arthritic joints and does not affect platelets in the blood.

One special advantage of acetaminophen is its stability in liquid preparations. While aspirin must be administered in tablet, powder, or suppository form, its substitute can be given by spoon or dropper, a big help in caring for children and others unable to swallow any solid medication.

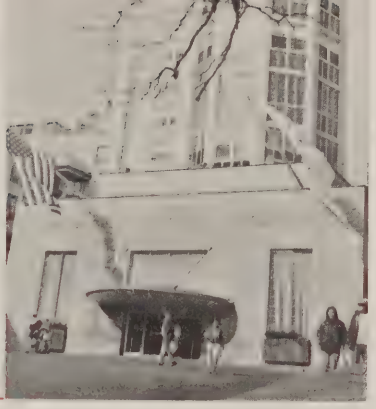
One day soon, aspirin itself may become available in liquid form.

However the drug is prepared, Dr. Rosow cautions the public to treat aspirin with the same respect as other medicines:

"People who think they can take an aspirin with much the same carefree attitude that they might have in taking a sugar pill could not be more wrong." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416



Tendonitis Commonly Strikes Athletes

(Concluded from Page 7)

doctors treating bursitis and tendonitis most often encounter elbow problems. Three "knobs" which can be felt at the elbow include the olecranon bursa, the lateral epicondyle, and the medial epicondyle.

The olecranon bursa, at the very point of the elbow, most commonly is affected by stress. Whereas shoulder bursitis might be caused by pure motion, elbow bursitis stems most of the time from repeatedly striking table tops and the like. Elbow padding and drug injections might suffice as a treatment. If infected, the bursa might have to be drained surgically and then treated vigorously with antibiotics.

The muscles that extend one's wrist and fingers attach to the lateral epicondyle, the knob on the outer side of the arm. Repetitive irritation of these tendons results in what is familiarly known as "tennis elbow." (See Page 2 editorial.)

"A bad backhand in tennis can cause that condition," Dr. Chandler said. "Using a racket with a lower string tension and a larger handle helps. A racket that vibrates comparatively little on impact is a plus. So are anti-inflammatory drugs."

The medial (or inner arm) epicondyle links with the muscles that bend the fingers and wrist. Tendonitis affecting these muscles is often called "golfer's elbow." The irritations arise when golfers flick their wrists on completing their swing.

Tennis players can develop golfer's elbow by twisting the wrist too much while striving for slices and spins on the ball.

On the hip, the bony prominence where bursitis or tendonitis most commonly occurs is situated next to the head, or ball, of the thigh bone, the longest bone in the body. Muscles and tendons course over the prominence (called the greater trochanter), then extend down to the knee.

Dr. Chandler recalled a patient, a young housewife, who came to him complaining of hip discomfort that had already spanned several weeks. The woman and her husband were planning a vacation and did not know whether to proceed with the arrangements.

"The patient had a young child and developed a habit of balancing the youngster on her left hip so that her right hand would be free to do other things," the doctor related. "The child's weight caused tendonitis in the mother's hip."

The first step toward overcoming the affliction was to break the mother's habit of toting the child the way she did. Oral anti-inflammatory agents also were prescribed.

People with one leg longer than the other, perhaps 10 percent of the population, may be more susceptible to bursitis or tendonitis in the hip.

Other likely candidates include obese, middle-aged or older women who habitually sleep on one side of the body.

The much heard expression "housemaid's knee" refers to an inflammation of a bursa over the front of the kneecap (patella). This type of bursitis almost always results from the punishment incurred by working or crawling on the knees.

Basketball players sometimes suffer tendon irritations between the kneecap and the leg bone (tibia) as a result of the shock of constant jumping. The condition is appropriately labeled "jumper's knee."

The Achilles tendon, running from the heel bone to the calf muscle, also endures abuse from overuse. A heel lift (like on a jogging shoe) to put the foot into almost a tiptoe position would relax the tendon.

And at the back of the heel there is a bursa which ill-fitting ladies' shoes sometimes inflame through friction. Like tennis elbow, housemaid's knee, and jumper's knee, this foot problem also has a nickname. It's called a "pump bump." ■

Dr. Hugh Chandler demonstrates how muscles can become pinched in the shoulder, resulting in tendonitis.

MGH News

Vol. 41 No. 1 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS January–February, 1982

Doctors Study New Way to X-ray Blood Vessels

Computers Facilitate Access to Patient Care Records

At the turn of the century, many physicians saw little need to record any medical data on patients making office or clinic visits.

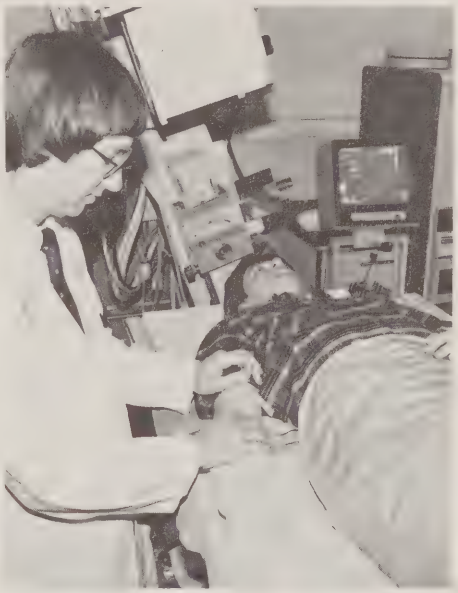
Fifty years ago, the information noted on such ambulatory, or outpatient, appointments filled only a few lines.

Since then, the increased complexities of medical treatment and the sheer weight of information on each patient have made record keeping an integral part of every medical practice.

But even the most elaborate manual system of paper filing eventually becomes overloaded.

The medical record of one patient

(Continued on Page 2)



Dr. John Hesselink of Neuroradiology prepares to insert a thin tube into an arm vein as a first step in digital subtraction angiography.

For a number of years doctors have looked to data from an X-ray procedure called angiography to assess blood vessel disorders and map corrective surgery.

Ordinary X rays reveal bone in excellent detail, but radiologists have to inject contrast material into the bloodstream to enable vessels to appear on film.

A resulting series of pictures termed an angiogram (or arteriogram) permits physicians to see exactly where a problem lies and determine the scope of the difficulty.

While angiography provides definitive information, the test at the same time causes discomfort to the patient. It is also expensive, requiring a couple of days in the hospital, and involves a slight risk to the patient.

Today, MGH neuroradiologists and vascular radiologists are trying out a device which furnishes the same data as conventional angiography but under a much different set of circumstances.

The new procedure, called Digital Subtraction Angiography, does not hurt, costs only one-sixth as much as the conventional, poses less risk, and requires no hospitalization. The patient does not even have to undress.

Assigned by Drs. Juan M. Taveras, Chief of Radiology, and Kenneth R. Davis, Chief of Neuroradiology, to help evaluate the new technique in head and neck vessels, Dr. John R. Hesselink of Neuroradiology cautioned that the system reached its practical stages only one or two years ago. "There is much to be learned about its capabilities and weaknesses," he said.

During its MGH trial program which began only a few months ago,

(Continued on Page 4)

EDITORIAL:

Academic Industrial Research—Revisited

Along with the frost and snow, a harbinger of winter is the annual meeting of the MGH Scientific Advisory Committee (SAC). The members of SAC are internationally known scientists who give up several days each December to come to the MGH. As the committee name suggests, their purpose is to advise the hospital's Trustees on research activities. This year's task: to examine the cooperative role of industry and academia in science.

The timing is obvious. With governmental support falling off, hospitals and universities are looking elsewhere, mainly to industry. A multimillion dollar contract from Hoechst, an international chemical company, to aid one new department has made the MGH a leader.

SAC members listened to two MGH investigators describe their own

(Concluded on Page 2)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
Joseph B. Martin, MD, *Interim General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIAL: *(Concluded from Page 1)*

Academic Industrial Research—Revisited

laboratories' agreements with industry. And then they heard Harvard University President Derek C. Bok outline his views about such relationships.

President Bok took a middle ground between those who condemn and those who lavish praise on these arrangements. First, he believes industry will supplement but not replace government support. He said he considers that contracts like the one between MGH and Hoechst are "constructive to academia. [. . . In view of increasing restrictions on government-funded research.] these agreements have a potential for providing more and not less freedom to university researchers."

On the other hand he cautioned that other contracts must, like the Hoechst agreement, "be vigilant to avoid restrictions on academic research. . . . Publication rights have to be guaranteed with no delay beyond a reasonable period for patent rights to be submitted."

Where President Bok saw trouble was "not from industrial support from particular firms but the increasing tendency for scientists to themselves have an interest [financial] in companies." He sees three dangers from this: 1. The professional with a financial stake has strong motivation to benefit the company and thereby himself through an increase in the value of stock. 2. Secrecy to safeguard the competitive position of the firm. 3. A possible negative effect on the image of science and a source of envy and divisiveness with academia. "The dangers," President Bok said, "are substantial."

To combat these dangers the Harvard University leader offered guidelines: 1. The traditional limit on the time of academicians on outside activities, a suggestion he concedes is difficult to enforce. 2. The traditional proscription against secrecy and the usual guidelines on the use of graduate students. 3. A prohibition on taking executive roles in companies while carrying out academic work. 4. Universities should consider banning exclusive licenses to any firm in which a professor holds a significant stock interest. An even bolder step, he said, would be to copy federal conflict of interest regulations and prohibit professors from holding a significant share of the stock of companies with research programs that overlap their own research. While stopping short of advocating these restrictions, he did observe that "rules of this kind deserve our serious consideration."

One member of SAC offered similar suggestions during the SAC discussions. The MGH community—and hopefully many others—will debate the issues. It must.

Computerized Data System Performs Many Functions

(Continued from Page 1)

may contain not only entries from several physicians but also lengthy notes from other health care providers, such as nurses, dietitians, and social workers. Then, of course, results of laboratory, X-ray, and other vital tests must be listed.

The responsibility for ambulatory care is shifting increasingly from the solo practitioner to coordinated teams of specialists.

In some ambulatory settings the work of extracting specific data from a record can sometimes be likened to chipping away at a mountain.

Since the late 1960s the MGH Laboratory of Computer Science has developed computer technology applications to streamline medical record keeping.

What has emerged is a powerful Computer-Stored Ambulatory Record system adaptable to the needs of any ambulatory health care organization.

A health provider can use the system, called COSTAR, to register patients, schedule appointments, store and retrieve virtually limitless medical data, and even generate bills for services. Fashioned in modular form, COSTAR includes a security module that guards against unauthorized access to the stored data.

The MGH computer specialists developed the system initially for the Harvard Community Health Plan, a large prepaid clinic in Boston. So successful was this COSTAR prototype that in 1975, six years after its installation, its sponsors proposed the designing of versions with wider functional capabilities to meet the needs of diverse ambulatory services.

The MGH Laboratory, directed by Dr. G. Octo Barnett, worked with the Digital Equipment Corporation and the National Center for Health Services Research to produce a COSTAR system that operates today in England, Argentina, Canada, Sweden, Finland,

Photographs: Pages 1, 3 (lower), 4, 7, 8, Myron Daniels; p. 3 (upper), courtesy of Dr. G. Octo Barnett; p. 5 (upper), courtesy of Dr. John R. Hesselink; p. 5 (lower), 6 (upper), courtesy of MGH Dermatology Department; p. 6 (lower), courtesy of Dr. Martin S. Hirsch.

COSTAR produces medical record information both on a screen and on paper.

Colombia, Japan, and many areas of the United States.

Since 1979, The Mitre Corporation has assisted in disseminating and supporting the system under a government contract.

The installations, at last count numbering 43, range from a few centers which use only accounting functions to establishments employing the full seven-module arrangement.

In California, where about 40 percent of the installations are situated, five clinics are served via telephone lines by a single central computer. In Maine, a small rural medical clinic uses the system by telephone connection with a computer at the MGH.

One medical group in England uses COSTAR solely for occupational health purposes. The stored data relate primarily to the history of workers' exposure to potentially toxic substances employed in industry.

Most COSTAR users, however, rely on the system to furnish information that will help them fulfill the general health needs of their patients.

COSTAR can remind a doctor what patients he is scheduled to see on a particular day. On the eve of those visits the computer will issue paper printouts summarizing the problems, diagnoses, test results, and treatments, including operations, that each patient has had.

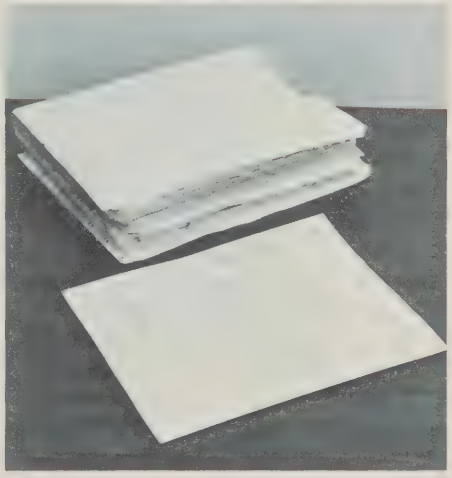
The summaries may also stipulate the periodic tests that are necessary, such as X rays, pap smears, breast exams, and stool studies.

When the doctor arrives for the day's work, the information, filling only one or two pages, already lies on his desk.

"Not only is the practitioner released from the often arduous task of leafing through countless pages of a manual record," said Dr. Barnett, "but if, for some reason, others in the office or clinic need access to the record, the computer can accommodate them. It can serve many simultaneously."

The users establish their own set of rules on how the computerized system shall serve them. COSTAR obeys the rules through a special internal computer language called the Massachusetts General Hospital Utility Multi-Programming System, or MUMPS (*MGH News,* June–August 1974).

"There is virtually nothing a paper record can do that COSTAR can't," said Dr. Dewey Jackson, an internist at Boston's North End Community Health Center, which installed the system a year and a half ago.



Much of the data a doctor needs from a record as voluminous as the one above can be provided quickly by computer on one or two sheets of paper.

Occupying three floors of a converted church structure, the center receives 60,000 patient visits annually. Its paper record file was growing at an enormous rate when COSTAR arrived.

Dr. Jackson finds the automated setup most advantageous when patients are being followed up for multiple, complicated problems that require many tests and an array of medications.

"When you're working with a large paper file handled by any number of people, you can easily overlook somebody's note recommending further evaluation of some condition," he said. "But COSTAR doesn't forget. It provides reminders."

Suppose health authorities ordered a drug removed from the market. COSTAR could quickly provide a list of every patient using that drug, thus enabling the prescription to be changed.

What if a pharmacy called for permission to renew a prescription? The doctor could ask COSTAR to confirm the type of medicine given as well as the instructions for use. The doctor's permission could be given without delay.

If a physician were examining a patient for high blood pressure and wanted only the individual's previous blood test results, the doctor could request that information alone, and it would flash quickly onto a screen.

At the MGH, several members of a staff group practice called Internal Medicine Associates have used COSTAR for the past three years.

Dr. Allan H. Goroll, who supervises the system for the I.M.A., said this application of COSTAR initially was funded as a tool for teaching and evaluating the progress of residents and interns who were learning to give primary care.

"It was a way of surveying their work to assure quality," Dr. Goroll said, "and also to make certain that the types of patients they were seeing were common to a primary care practice."

For example, the computer data base may be surveyed from time to time to monitor whether the physicians have performed a stool examination that serves as a screening test for cancer of the colon.

The computer may be asked to identify the number of patients over 40 years old treated by each young doctor. Then, a printout would indicate how

(Concluded on Page 4)

Digital Angiography Eliminates the Risk Of Harm to Artery

(Continued from Page 1)

the device is being shared on a 50–50 basis by Dr. Hesselink's team and by the vascular specialists under Dr. Christos A. Athanasoulis, Chief of Vascular Radiology.

Because the latest procedure involves a radically different method of injecting contrast material, the possibility of triggering a stroke is reduced substantially.

In conventional angiography, the radiologist threads a flexible tube (catheter) through an artery (femoral) in the groin to the site under study. Then the specialist injects the contrast material through the tube.

The potential risk lies in the manipulation of the catheter. It is made to travel all the way to the carotid arteries, the two principal large arteries in the neck. On the way the tube could knock fatty deposits from the inner lining of a vessel. Later, these deposits could wedge at a narrower point up the line and block blood flow.

If the radiologist were doing a carotid artery study using the digital subtraction method, he would insert the catheter in an arm vein, not an artery.

The catheter would be extended to the upper body's main vein (the superior vena cava) for an injection into the blood at that point.

Since blood that needs more oxygen courses through the superior vena cava to the heart, the contrast material would travel along, going through the heart, lungs, back to the heart, and then out into the aorta, the body's main artery. In seconds, the material, or dye, would reach the carotid vessels, and the X raying would begin.

At no time would the catheter have proceeded beyond a vein and into an artery where blood pressure is higher.

Technologist Julie Jelinek at the controls during a digital angiography test

Also, in its travels, the contrast material would dilute somewhat. This in itself would contribute to the patient's comfort.

The subtraction aspect of the new technique helps the radiologist to view the target vessels.

Dr. Hesselink explained that the system takes a series of X-ray pictures without the contrast fluid, then a similar number after injection of the fluid. A computer, which processes the data in digital, or numerical, fashion, proceeds to subtract the first pictures from the second. Any bone or soft tissue covering the target vessel would be eliminated in a resulting third set of photos, and only the tissue containing the contrast would be visible.

Digital subtraction angiography has been tested at the Universities of Wisconsin and Arizona and at the Cleveland Clinic. Of several thousand patients who underwent the procedure at Cleveland, 70 percent were evaluated for carotid problems. In about 80 percent of the published carotid studies, good diagnostic tests resulted.

Other neck pictures were unacceptable because the patients moved during the X rays. Absolute stillness—not even swallowing—for about 30 seconds is demanded of the patient, or the X rays will blur.

To make sure that a patient's body will quickly dispose of the contrast material after the examination, doctors often check kidney function. The finding of an abnormally high level of a waste product called creatinine might call for using less contrast fluid or avoiding the angiography.

COSTAR

(Concluded from Page 3)

many patients received the stool test and how many did not.

"The data give us some idea of how well the doctors are carrying out their responsibilities in preventive medicine," Dr. Goroll pointed out. With added funding, shared by the government and the hospital, the I.M.A. soon will enjoy full COSTAR services.

Dr. John Stoeckle, Chief of the Medical Clinics, said the hospital's manual files will continue up to date. "Features of the history and physical findings on patients will be entered into COSTAR, along with the personal observations of the doctors," he said. "And copies of COSTAR data can be supplied to the record room for inclusion in the paper files."

Dr. Barnett of the Laboratory of Computer Science remarked that "we may not live long enough to see totally computerized hospital record keeping, but we will see a gradual transition.

"We must make sure that this changeover does not make medical care less humanistic. All we're trying to do is remove the tedious and laborious work that is such a large part of medicine. Then the physician can concentrate on what he does so well, and that is care for his patient." ■

The uses for the new technique are many. Dr. Athanasoulis pointed out that when a person arrives at the hospital's Emergency Ward suffering multiple injuries from an accident, it is vital to have a quick evaluation of the main artery in the chest, abdomen, and pelvis. "This is an ideal use for digital," the doctor said. "We can do the studies quickly and safely."

In patients suffering from high blood pressure, digital can determine whether the illness is kidney-related. After a kidney transplantation, doctors can employ digital to make certain that the connections to the donated organ remain secure.

Digital tests are just the thing to follow the results of a new procedure being employed with conventional angiography to eliminate blockages within arteries. In the technique called a "balloon angioplasty," a catheter with an inflatable balloon at the tip is guided to the problem site, and the tiny air bag is inflated to clear the channel (*MGH News,* April 1981).

These digital tests would reduce risk, cost, and discomfort compared to standard angiography.

Sometimes digital will do what conventional cannot. Dr. Athanasoulis told of a middle-aged woman at another large Boston hospital who, after surgery for several blood vessel problems, was thought to have a carotid abnormality. Because of the surgery, the patient could not tolerate the usual angiography.

Digital angiogram of the principal neck arteries reveals a serious narrowing (see arrow).

"Knowing that we had the digital equipment, the woman's physician called and asked if he could send her to the MGH for the test," Dr. Athanasoulis related. "We obtained excellent, diagnostic images of the carotid vessels showing a stenosis [narrowing] in one of them, and within 45 minutes after arrival the patient was en route back to the other hospital for treatment."

Often, digital will show that nothing is amiss. A routine chest X ray at the MGH disclosed a strange shadow on the chest of a 35-year-old man. The cloudy area could have signaled an aneurysm, or outpouching, on a blood vessel wall. Digital ruled out the aneurysm.

As physicians at the MGH and elsewhere gain more experience, they will be better able to evaluate the best uses for digital.

Machines that will perform digital subtraction angiography on the pulsating heart, taking as many as 30 X rays a second, already are being tried out elsewhere. With only slight modifications, the system now in use at the MGH can be made suitable for such studies.

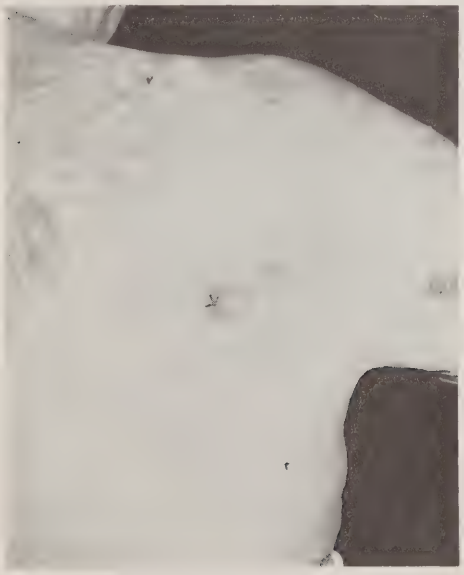
Basically, however, digital subtraction angiography remains in its infancy, said Drs. Athanasoulis and Hesselink, who are also Professor and Assistant Professor of Radiology, respectively, at Harvard Medical School.

They said that in the ensuing months digital studies conducted at the MGH will be closely monitored and compared with the findings of conventional angiography as well as sophisticated noninvasive tests to make sure the new technique is absolutely accurate and misses nothing. ■

Shingles: The Stowaway Disorder

Most people experience chicken pox by the time they have grown up.

Red blotches appear first on the skin followed by blisters. These dry up in a few days, and scabs then cover the area. In another two to four days, these, too, vanish.



The sores of shingles on a patient's back and arm

In otherwise healthy children, perhaps the principal concern of physicians and parents is that patients will succumb to a temptation to scratch, thus inviting a possible secondary infection.

Most parents think that their child gains lifelong protection from the guilty virus after a bout with chicken pox.

Not so.

Although a youngster's recovery from this usually mild infectious illness may be quite uneventful, the virus (also known as varicella) may linger in the body, erupting possibly many years later as a painful condition known as shingles.

"Shingles presents a much different picture from chicken pox even though the two stem from the same organisms," said Dr. Martin S. Hirsch, Director of the MGH Virology Laboratory.

"The lesions, or sores, produced by shingles are more localized and associated with much more pain. The pain can continue long after the lesions have healed."

The manner in which chicken pox and shingles originate can explain why one illness is mild and the other is not.

In the pox, the virus is inhaled and travels through the respiratory system, then the bloodstream, to various parts of the body. In shingles, the organism emerges from nerve roots after lying dormant from the time of an episode of chicken pox previously experienced by the patient.

"The pain from shingles, also known as herpes zoster, comes from the nerve involvement," Dr. Hirsch said. "Some patients with the disease later suffer from a type of nerve pain called postherpetic neuralgia. It can cause excruciating distress."

The virus may lie latent for 50 or 60 years in bundles of nerve cells (ganglia)

(Continued on Page 6)

Chicken Pox Always Precedes Shingles

(Continued from Page 5)

situated along the back of the spinal cord. When the disease activates, it customarily follows the path of a nerve involved in feeling or sensation.

Usually the first indication of shingles is pain. It may precede any redness on the skin by several days. Blisters and scarring follow.

Unlike the general distribution of sores that characterizes chicken pox, the blisters of shingles appear on only one side of the body. This is because the nerve involved serves one side or the other but not both.

Studies have shown that people in their later years are more susceptible to shingles and to persistence of its irritations.

Dr. Hirsch said the body's natural disease-fighting system apparently helps to keep the virus in check during one's early and middle years, but as old age creeps up, the immunity that had been rendered tends to wane.

Tables reflecting the frequency of shingles indicate that the disease strikes 1 person per 1,000 between the ages of 10 and 19 compared to 10 people per 1,000 between ages 80 and 89.

The illness affects males and females equally, and no climate or country seems to escape the disorder.

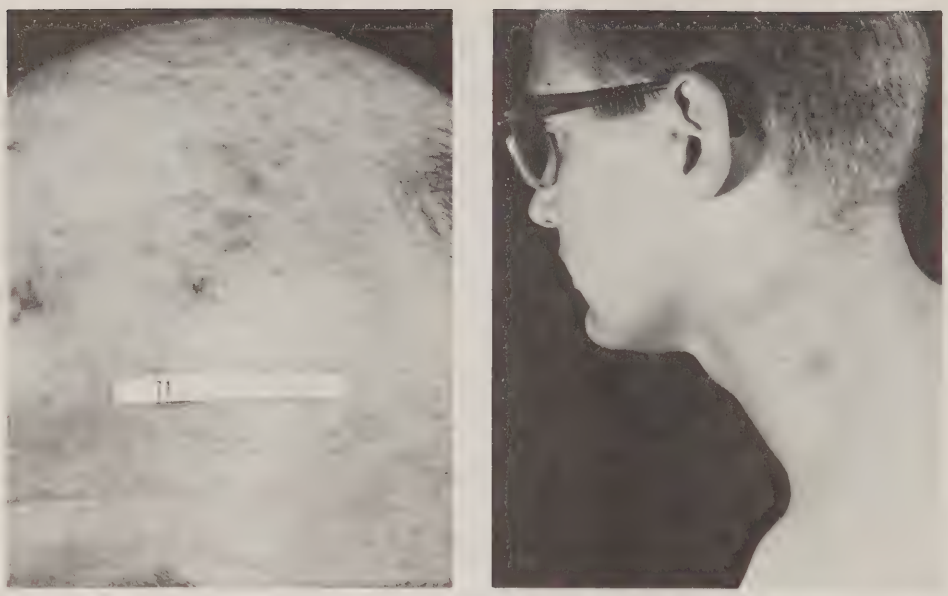
Dr. Hirsch emphasized that shingles is never a primary infection. One does not contract the disease without first having caught chicken pox.

This would seem at first to classify shingles as an adult illness. However, if a child contracted chicken pox at 6 months of age or so, he could get shingles at, say, age 3.

Suppose a child were under treatment for some form of cancer. Drug or radiation treatment could suppress the body's immune system, thereby releasing the virus that causes shingles. Drugs given to a transplant patient to prevent rejection of the newly received organ also might indirectly activate the latent virus.

Special efforts have been made to protect high risk children, particularly those with leukemia, from developing chicken pox.

The Atlanta-based, federally operated Centers for Disease Control conducted pioneering studies which demonstrated the protectiveness of a serum called zoster immune globulin. It contains antibodies from samples of blood volunteered by people recovering from shingles, or zoster.



Patients afflicted with shingles on the head (left photo) and on neck (right photo)

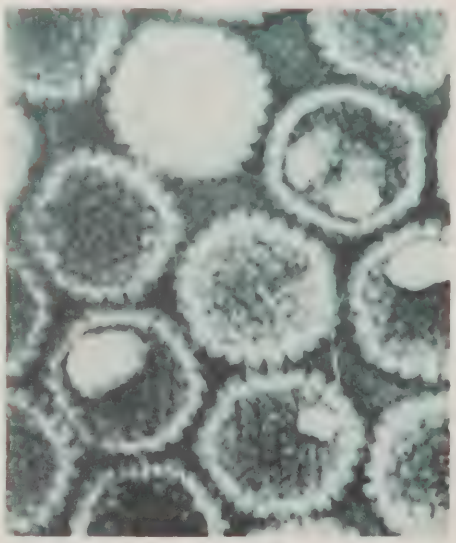
A nationwide network of physicians controls the supplies of globulin. They make it available to high risk children who have been exposed to chicken pox and have no previous history of it.

With the serum protection, recipients either escape the illness entirely or contract only a very mild form.

The Massachusetts State Laboratory Institute in Boston produces the zoster immune globulin for the entire nation.

One might well ask, "If the serum can prevent chicken pox, why not give it to all children?" The answer is that the protection is only temporary, lasting perhaps six weeks.

In a high risk patient, even the brief protection can be invaluable during a crisis.



The chicken pox-shingles virus can be seen with an electron microscope as hexagonal-shaped organisms.

In healthy young children, however, the disease is normally so mild they would actually be better off having experienced an attack.

"If a person goes through childhood without getting chicken pox, he can still be afflicted as an adult," Dr. Hirsch pointed out. "And in adulthood, the disease can be devastating."

He said that increasingly at the MGH doctors encounter adults who grew up free of the illness and then contracted it from a son or daughter. While the child's condition was usually mild, the parent's was often accompanied by life-threatening pneumonia.

A vaccine against chicken pox has been developed by a group of scientists in Japan and is being used widely there. Trials of the vaccine also are under way in the United States.

Some people fear, however, that since it is made from live virus the vaccine might in itself cause a latent infection that could result in later difficulties.

In the vast majority of patients, shingles, while painful, does not threaten life. But depending on the course taken in the body, the disease can affect motor function, the lungs, bladder, bowel, ears, and even damage vision.

Dr. Hirsch, who is also Associate Professor of Medicine at Harvard Medical School, said treatment for shingles in otherwise healthy persons is aimed principally at relief of pain. The drugs being prescribed range from aspirin to morphine.

A federally funded national collaborative of more than a dozen medical centers, including the MGH, has made

Emphysema Destroys Elasticity of Lungs

Few high-altitude mountain climbers would embark on a new venture without an ample supply of oxygen.

At a height where the air thins and places increased demands on physical stamina, the availability of oxygen often becomes the decisive factor on whether an expedition proceeds or turns back.

One does not have to look far to appreciate the torment that lack of oxygen can inflict upon the human body. Just talk to someone with advanced emphysema.

Hungering for air because of a destruction of lung tissue, he experiences the same effects as the high-altitude climber except that while the sportsman thinks he may be nearing the "top of the world," the patient is trying to dress, shave, or merely trudge down the block.

Just to breathe he must call upon all available muscles of the neck, chest and abdomen.

The most common life-threatening chronic disease in the United States, emphysema destroys the elasticity of the lungs and therefore their ability to inhale and exhale air, separate oxygen from it for the body's use, and expel unwanted carbon dioxide.

As the desperate struggle to continue this vital gas exchange goes on, tiny air sacs (alveoli) in the lungs at the same time collapse or balloon tremendously in size. (In Greek, the word emphysema means inflation.)

Often occurring in association with chronic bronchitis, emphysema takes 35,000 lives in this country each year. In addition, the disease contributes to the deaths of another 30,000 people, many from heart disease.

"Coronary artery disease and lung disease have a common denominator, and that is smoking," said Dr. Homayoun Kazemi, Chief of the MGH Pulmonary Unit. "Emphysema is estimated to be 19 times more common among cigarette smokers than among nonsmokers."

One reason, he explained, is that smoke in the lungs causes an overproduction of a group of cells called macrophages which attach to lung tissue. They normally gobble up foreign organisms, but the smoke so stimulates the cells they also attack normal tissue.

"If you wash out the cells from the lungs of a smoker," the doctor said, "you would discover not only many more macrophages but also that the cells had become much more potent, or charged up, than normal."

Studies in recent years also have implicated cigarette smoke in the failure of two enzymes in the lungs to maintain a delicate balance.

One substance, called elastase, tends to destroy a key component of the air sacs which gives them their resiliency. But the other enzyme, called anti-elastase (or alpha$_1$-antitrypsin), normally counteracts the destructive agent. Smoke apparently prevents the anti-elastase from doing its job.

Marked by gradually worsening breathlessness, emphysema usually is first detected in people in their late 40s. However, the disease does develop occasionally in younger individuals—even toddlers—because of a genetic disorder leading to a deficiency of alpha$_1$-antitrypsin (*MGH News,* June–August 1972).

Many people complain of having a cigarette cough. Actually, the cough comes from bronchitis, an inflammation of the tubes (bronchi) which carry air to the lungs from the windpipe (trachea). When a cough persists for at least three months during each of two successive years, it is then chronic bronchitis.

Dr. Kazemi said the coughing, coupled with sputum from the bronchial tubes, makes bronchitis easily diagnosable, and much can be done for the condition. "We have drugs to stop the muscle spasms, manage the secretions, and dilate the tubes," he said.

As for emphysema, a computer-based pulmonary function test (*MGH News,* December 1978) provides highly accurate data on capabilities of the lungs. As part of the assessment of a patient's status, values derived from

(Concluded on Page 8)

encouraging progress, however, in developing effective drugs against the zoster virus itself.

Used only in high risk patients, a medication called vidarabine has proved beneficial if administered in the first 48 to 72 hours of the outbreak of illness.

"Studies show that vidarabine leads to less pain, fewer complications, and earlier healing," Dr. Hirsch said. "We use it routinely in our high risk zoster patients."

Another drug, called acyclovir, appears to hold promise for antizoster treatment. Much less toxic than vidarabine, acyclovir is currently being studied in high risk groups to treat zoster, or shingles, during peak danger periods. Some researchers have shown that interferon also may help in treating the disease in immunosuppressed individuals.

"Clearly, much is being done on several fronts to help combat this disease," said Dr. Hirsch. "One day soon, we may have several effective treatment options." ■

If Patricia Hill, posing before a gamma camera, had emphysema, an image of her heart relayed onto the screen of a radionuclide scanner could be checked by Dr. Michael Schneider for possible heart damage.

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114
Address Correction Requested

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Emphysema Can Injure the Heart

(Concluded from Page 7)

the test, which involves exercise, are compared to the known responses of healthy individuals.

"Some patients with particularly severe emphysema are found to retain high levels of carbon dioxide," said Dr. David J. Kanarek, Director of the MGH Pulmonary Function Laboratory. "We think this may reflect abnormalities in the brain's respiratory control centers. There could be a genetic basis for the condition."

Patients with carbon dioxide retention take 22 or 23 breaths per minute, several more than the average emphysema patient without the carbon dioxide problem.

Physicians at the MGH instruct patients on a beneficial method of breathing. By taking a quick breath, then exhaling slowly with lips pursed, an individual can reduce strain on the lungs and can feel more relaxed.

As emphysema inflates more and more air sacs in the lungs, the chest often takes on a barrel-shaped appearance. Muscles used in respiration cannot contract as well as before. Dr. Kanarek said that certain drugs now available prevent muscles from tiring as quickly.

During sleep many emphysema patients endure profound reductions of oxygen in their body tissues (hypoxia). On awakening, the patients feel uncomfortable, fatigued, and headachy. Oxygen kept at the bedside and inhaled when needed has proved helpful.

As air sacs are lost to emphysema, tiny blood vessels (capillaries), which receive oxygen in the lungs, also become useless. Blood backs up through the pulmonary artery to the right ventricle, a pumping chamber of the heart, causing great strain.

During the past year, Drs. Kazemi and Kanarek have joined a number of MGH cardiologists in studying emphysema's effects on the heart.

After injecting a radioactive substance (technetium 99m) into a patient's arm, the doctors use a device called a radionuclide scanner to take pictures tracing the course of the material through the heart. In this way, the investigators have seen how the right ventricle can become very abnormal upon minimal exertion by the patient. The doctors hope their studies will find a way to deal with this problem.

In other emphysema research, the Pulmonary Unit is making use of radioactive tracer chemicals produced by the MGH cyclotron.

By watching the course of one tracer, nitrogen$_{13}$, which is inhaled by the patient, investigators hope to figure out exactly how the disease is harming the lungs. The chemical's radioactivity is very short-lived. The risk to the patient is no greater than that of a conventional chest X ray, and there is no discomfort.

Dr. Kazemi's laboratory also is using nitrogen$_{13}$ to develop a method of reducing distension of the lungs so that the chest is not as full and the patient does not feel so short of breath.

The researchers believe they can realize their goal by means of some kind of "puffing" device which would artificially vibrate air in the lungs, thereby keeping the airways open.

Dr. Kazemi, who is also a Professor of Medicine at Harvard Medical School, said the most important step in fighting emphysema is to stop insulting the lungs. That means: Stop smoking! Although many chemicals pollute the air and contribute to chronic obstructive lung ailments, tobacco smoke containing hundreds of different chemicals represents the greatest single cause of emphysema.

In comparison to a healthy person whose lungs contain 300 million tiny air sacs, an individual with emphysema may have to struggle along with only 100 million.

"New air sacs do not develop in a person after the age of 8 or 10," Dr. Kazemi said. "But if someone contracted emphysema from smoking and stopped the habit, the degenerative processes probably would also stop. Even sacs which had become partially abnormal could stabilize." ■

Using a spirometer, Technician Gary Miller measures the breathing capacity of Marianne Murphy's lungs.

MGH News

Vol. 41 No. 2 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS March, 1982

Timely Surgery Offers Protection Against Strokes

Eye Tumors Shrink From Proton Beam Radiation Exposure

The five patients traveled from Missouri, Illinois, Ohio, New York, and Canada.

A tumor had cost each the sight of one eye, and now a growth found in the other eye threatened each person with total blindness.

They came to Boston hoping that their remaining vision could be saved by a treatment pioneered by specialists at the Massachusetts Eye and Ear Infirmary (M.E.E.I.) and the MGH.

For many years, the standard method of treating malignant melanomas, the type of eye tumor affecting the five individuals, was to remove the eyeball (enucleation). At the time, this offered the best protection against a spread of tumor cells.

Before coming to Boston, four of the patients had undergone an enucleation of the first eye that became diseased. The fifth patient had treatment of one eye with cobalt plaque irradiation which failed. Doctors decided not to remove the hopeless eye because of the man's advanced age.

By the time the latest misfortune befell the patients, their physicians had learned of the new technique in Boston. Called proton beam therapy, it held out hope of obliterating the new tumor while preserving the existing sight.

With the aid of physicists at Harvard University's Cyclotron Laboratory, an M.E.E.I.-MGH team carried out the

(Continued on Page 4)

In the early 1950s, a scientific journal published a Montreal neurologist's pioneering studies which shed important light on the relationship between stroke and carotid artery disease in the neck.

Reporting in the *Archives of Neurology and Psychiatry,* Dr. C. Miller Fisher defined the basic nature of the disease as atherosclerosis, a form of hardening of the arteries involving an accumulation of fatty material on the inner lining of vessels.

He also described how an occlusion, or plugging, of a carotid artery might lead to any one of several types of temporary attacks before a full-fledged stroke occurred.

It is conceivable, he wrote, that some day surgeons will find a way to reconstruct the occluded portion of the artery during the period of ominous fleeting symptoms.

Broken line across neck denotes where surgeon makes incision to clear carotid artery feeding blood to brain.

Dr. Fisher, who has been at the Massachusetts General Hospital since 1954, did not have to wait long for his prophecy to come true.

His observations led surgeons at a number of centers to devise repair techniques. In the early 1960s he began to work with Drs. Robert G. Ojemann of the MGH Neurosurgical Service; William H. Sweet, then Chief of Neurosurgery; and W. Gerald Austen, a cardiovascular surgeon and now MGH Chief of Surgical Services.

The removal of the obstruction is called a carotid endarterectomy (a surgical cleaning out of an artery).

As the technique of this operation was modified and perfected, it became apparent that many strokes could be prevented.

A publication by Dr. Ojemann, Dr. Fisher, and other colleagues in 1975 outlined the technical aspects of the operation, analyzed the indications for the carotid endarterectomy, and showed that strokes due to blockage in the carotid arteries could be prevented by this procedure with a very low risk.

How does the patient know if he or she has carotid disease? Most patients have warning spells called transient ischemic attacks (TIAs). These can be a temporary loss of vision in an eye (like a shade descending and then a few seconds or minutes later ascending), weakness or numbness in an arm, leg or the face, or difficulty with speech.

Unfortunately, perhaps as many as 20 to 30 percent of patients with carotid disease have a stroke with no warning. However, the doctor may be

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
Joseph B. Martin, MD, *Interim General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

Choosing a General Director

Since 1962 the MGH has chosen General Directors from within its walls. The rationale is clear. The MGH is a large, complicated institution. To learn its complexities demands someone with at least a rudimentary awareness of what makes this hospital unique: the unusual nature of its table of organization, the relationship with affiliated and nearby institutions, the variety of patient care settings and models, the vast research endeavor, and the educational effort with its separate Institute of Health Professions. The realities of learning about and of learning to work with these diverse elements are significant.

With such reasoning uppermost, most knowledgeable observers expected an MGH-trained physician to succeed Dr. Charles A. Sanders as General Director. By now MGH watchers who made such predictions know they guessed wrong. The Board of Trustees turned to Dr. J. Robert Buchanan, President of Michael Reese Hospital in Chicago. Why? First, one has to examine the reasons behind the traditional mode of selection. While homegrown General Directors know the organization and the players, at the outset they generally lack knowledge about hospital administration, governmental regulations, health care insurance, and other hospital-related fiscal matters, and about the intricacies of academia. In 1982 these issues predominate and seem to be much more important than starting with a detailed knowledge of the MGH. In other words, the trustees believe that a new chief executive officer will find the MGH itself less an enigma than the external world which impacts and threatens it.

In Dr. Buchanan, the trustees have clearly chosen a man who knows hospital administration. He has spent the last five years as the head of a large and distinguished general hospital in a major city. Michael Reese is also like the MGH in that it is a teaching hospital with research commitments. As former Chairman of the Board of Trustees of the Illinois Hospital Association, Dr. Buchanan became familiar with the intricacies of regulation and the workings of bureaucracy at the federal, state, and municipal levels. As Chairman of the Board of Trustees of Insurance Risk Management Services Inc., he delved closely into malpractice insurance. Before going to Michael Reese, he gained experience in depth in academic matters as Dean of Medicine at Cornell University for seven years. An endocrinologist, he is licensed to practice medicine in five states from New York to California.

In fact his background for leading a major teaching hospital in these troubled times is extraordinary. So much so that people who have read his curriculum vitae expect much. What about his ability to think under fire? A biography provides little clue to that. But those who heard him articulate his views last month to the Boston news media came away believers. From his eloquent plea for federal support for basic research to his obvious grasp of major issues, he sounded as though he already belongs to and is of the MGH.

Neck Artery Noise Can Be Warning Of Stroke Risk

(Continued from Page 1)

able to detect with his stethoscope the first sign of trouble in a carotid artery.

With his listening instrument on the patient's neck to monitor blood flow, the physician may detect a noise or "bruit" if the flow were not normal.

The narrowed vessel might be discovered during a routine physical examination, while the patient was being seen for some unrelated disorder, or as the individual was being evaluated for an operation.

The question then would be: What does the bruit signify? A battery of noninvasive tests (some developed by the MGH) have been able to supply the answer in many patients (*MGH News,* June–August 1976 and November 1977).

Instead of indicating a carotid abnormality, the bruit might simply reflect another body activity such as a transmitted noise from the heart.

If there were indeed a carotid problem, the tests would help to show where it was, its nature, and its seriousness. For example, to the naked ear, bruits sound similar, but to sophisticated diagnostic equipment they form a pattern which can indicate early or advanced disease.

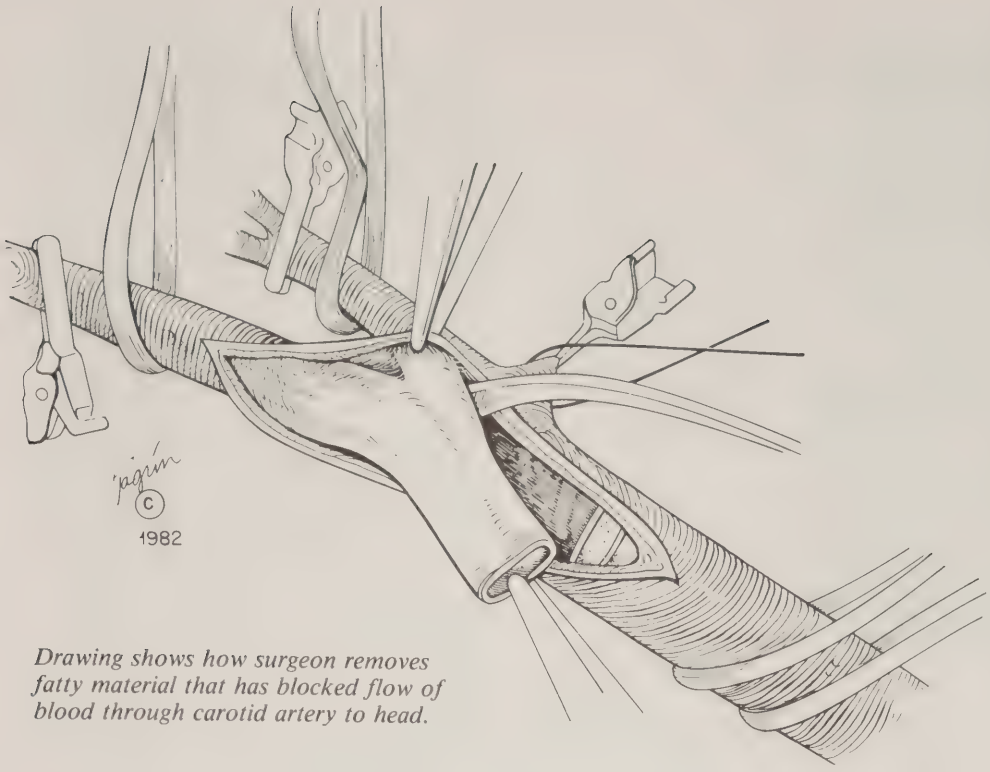
Even if a serious narrowing were noticed in one of the neck's two carotid arteries, corrective surgery might not be needed.

As each artery extends upward from the chest to deliver blood to the head, the vessel bifurcates, or divides into two branches, in the neck. One branch, called the internal carotid, feeds the brain and additional critical areas. The other, the external carotid, goes to the face.

An obstruction in the external branch would not cause a stroke. Other vessels channeling blood to the face would make up for the loss resulting from the blockage, and surgery would

Photographs: Page 4, courtesy of Michael Goitein, Ph.D.; p. 5, courtesy of Dr. Evangelos Gragoudas; p. 8, Chris Maynard.

Drawings: Pages 1, 3, MGH Medical Art Department; p. 6, United States Public Health Service; p. 7, National Kidney Foundation.



Drawing shows how surgeon removes fatty material that has blocked flow of blood through carotid artery to head.

be unnecessary.

Even in the more crucial internal carotid, the expected damage from a narrowing sometimes does not materialize because the vessel's healthy twin is able to take on an added burden.

Fortunately a new, even more sophisticated diagnostic test called digital subtraction angiography (*MGH News,* January–February 1982) has recently been developed. This intravenous test eliminates most of the risk associated with the previous X-ray test (intra-arterial angiogram) which was required when the noninvasive (causing no pain or potential harm) examinations suggested a serious lesion.

Now by studying data from noninvasive tests, anatomic information from digital subtraction angiography, and the patient's overall health, doctors can decide whether to repair a narrowed carotid artery surgically or rely instead on drug treatment.

Dr. William M. Abbott, Chief of Vascular Surgery at the MGH, believes that if a patient who is at risk for a stroke has no other problem that might affect life expectancy, such as cancer, the operation would be preferable.

"Although drugs are helpful in reducing TIAs and the incidence of stroke," he said, "there is no evidence to suggest that medication is as effective as returning the blood flow in the artery back to normal.

"This operation is causing a major impact on stroke, the number three killer in the United States today."

He said the rates of death and serious complications "for a carotid endarterectomy performed by competent hands are very small."

Either a vascular surgeon or a neurosurgeon may perform the procedure.

The operation to remove a blockage from a carotid artery takes two to three hours, but the most critical phase occurs when the blood flow in the carotid artery has to be temporarily stopped to remove the narrowing.

With the patient under general anesthesia, the surgeon exposes the diseased artery, clamps it to stop the flow of blood, and proceeds to make an incision at the trouble spot.

Throughout the operation an electroencephalograph (EEG) records the electrical activity of the patient's brain. During the cutoff of blood, the surgeon relies on the EEG to warn him when a shunt, or tube, is needed to carry blood around the obstruction.

Dr. Abbott said some colleagues feel the operation should always be conducted with a shunt, but "it is our feeling that except in certain circumstances we can do a better job without it." He estimated that only about 15 percent of patients really do require the temporary bypass.

The incision in the artery is usually closed with a continuous suture, but sometimes if the vessel is small, a patch, using a vein or synthetic material, is used.

Although the patient may leave the hospital feeling well within a week of the surgery, the postoperative care usually includes a brief stay in an intensive care unit.

Dr. Ojemann, one of the first surgeons to stress careful control of excessively high blood pressure after surgery, explained that after a carotid endarterectomy the patient's blood pressure must be watched very closely.

He said some individuals tend to have too low a blood pressure, and this must be corrected promptly. Others will have a marked increase in pressure which must be controlled just as promptly because a hemorrhage can be devastating. Fortunately both problems can usually be easily managed with drugs if there is careful monitoring.

Dr. Ojemann, who is Professor of Surgery at Harvard Medical School, stressed that these patients require a team approach both before and after surgery to reduce the risk to as low a level as possible. Many will have a blockage in the coronary arteries and will have a history of a heart attack.

He said the team should have physicians and other personnel with experience in the problems of vascular disease and include an internist or cardiologist, neurologist, neuroradiologist, anesthesiologist, operating room nurses, and recovery room personnel. "We have been fortunate to have all of these available to use," he said.

Patients who have undergone an endarterectomy clearly should minimize their risk factors for atherosclerosis. This means proper attention to diet, maintenance of blood pressure within a normal range, and elimination of cigarette smoking.

When these individuals are followed over several years, they are free of stroke, but there is a high incidence of heart attacks.

Both Dr. Ojemann and Dr. Abbott, who is also Professor of Surgery at Harvard Medical School, stressed that "listening to the blood flow in a patient's neck should be a part of every doctor's examination. It takes just a few seconds and carries no risk.

"Even if the physician finds that only 1 patient in 100 has stroke potential, the doctor will have performed a tremendous service to that individual and to the community as well.

"A stroke can be fatal to the patient or can be a very costly blow to society in general with the medical care and rehabilitation running into thousands of dollars." ■

Protons Strike With Burst of Energy

Richard Gentry, an MGH physicist, and Patricia McNulty, RN, review proton beam alignment films in preparation for treating a patient.

(Continued from Page 1)

treatments at the Cambridge installation. Each melanoma was bombarded with protons from the 160 million electron volt cyclotron.

Unlike X rays which are waves of electromagnetic energy, protons are positively charged particles of an atom's nucleus. They can be fired at a target with pinpoint accuracy.

Complex mathematical calculations enabled the cyclotron to generate an increased dose of energy at the disease point. Physicists refer to this high energy area as the Bragg Peak. The Bragg Peak was first used systematically by an MGH neurosurgeon, Dr. Raymond N. Kjellberg.

Each patient underwent five treatments over an eight-day period and was exposed to a total of 7,000 rad (a rad being a unit of energy absorbed from the proton beam per gram of tissue).

As time passed, it became apparent that the proton beam procedure had reversed the growth of the tumors in all five patients without sacrificing their ability to see.

One patient died a year or so later as a result of metastatic (spread of) disease. Until the day of his death, however, the sight continued in his other eye, treated with proton beams.

Since July 1975, when the new technique became available to patients with eye tumors, the M.E.E.I.–MGH team has treated more than 130 melanomas, most of them situated in the choroid, a layer rich in blood vessels at the back of the eye.

More than half the tumors were large, the diameter exceeding 15 millimeters, about 9/16ths inch, and a height of at least 5 millimeters, or 3/16ths inch.

Dr. Evangelos S. Gragoudas, Associate Director of the Retina Service at the M.E.E.I. and a leader in development of the proton beam program, said only four eyes had to be enucleated.

He estimated that after effective irradiation of the tumors 74 percent of the patients had the same degree of vision as before, and another 10 percent actually found their sight improved. In the remaining 16 percent, the vision deteriorated.

"When one treats tumors as large as the ones we encountered, some complications are bound to occur," Dr. Gragoudas said. "There are many vessels at the back of the eye, and some of them may bleed or leak serum."

Computer's view of eye with tumor (web of lines at lower left) in proton treatment position.

He said that since proton beam radiation has come into use for eye care the number of malignant melanomas that can be treated successfully has nearly doubled.

The treatments represent the combined efforts of Dr. Gragoudas from M.E.E.I., a physicist and a radiotherapist from the MGH Department of Radiation Medicine, and physicists at the Cyclotron Laboratory.

When Dr. Gragoudas has examined a patient and decided on the proton beam treatments, he operates to install a set of tiny metal rings around the tumor. The rings, made of tantalum, serve as markers for alignment later of the beam with the tumor.

Observing the surgical procedure to note the position of the rings and to make necessary diagrams in collaboration with Dr. Gragoudas is the MGH physicist, either Michael Goitein, Lynn Verhey, or Marcia M. Urie, all Ph.D.s, or Richard R. Gentry, who holds a master's degree in physics.

A meeting with the MGH radiotherapist, either Dr. John E. Munzenrider or Dr. Peter H. Blitzer, follows to round out the planning.

Dr. Goitein played a significant role in developing the technique for treating the tumor of the eye in humans.

Through a method established by Dr. Goitein, it is possible to align the tumor with the proton beam with an accuracy of 1/50 of an inch. Such accuracy assures that the healthy part of the eye will not be affected by the treatments.

Before they actually begin, the patient must go to the Cyclotron Laboratory for a simulated treatment. The laboratory staff under Andreas M. Koehler prepares the cyclotron for the various detailed technical steps leading to the treatment of the patient.

Computerized data enable specialists to find the best position for the patient, and a special plastic mask is made for the individual to wear during operation of the cyclotron.

A week or two later the treatments begin. Completely painless, they take only a couple of minutes each, although aligning the beam with the tumor may take about 20 minutes. The patient can go home when the series ends but must be examined periodically after that by an ophthalmologist.

Proton beams have served medicine for more than 20 years. Dr. Kjellberg began his pioneer work with proton beam radiation in 1961 to attack disorders of the pituitary gland (*MGH*

News, November 1969 and March 1973). His work has since expanded to include treatment of tumors and malformed blood vessels in the brain (*MGH News,* June–August 1979).

In the late 1960s, Dr. Milford D. Schulz, an MGH radiation therapist, suggested that proton beams might be helpful in treating infants for a form of eye tumor called a retinoblastoma. A committee headed by Dr. Robert N. Ganz, an MGH pediatrician, was organized to discuss the idea.

Subsequently, Dr. Ian Constable, a Fellow in Ophthalmology at the Retina Foundation in Boston, initiated formal research on the proposal at the request of Dr. Charles Regan, now Director of the M.E.E.I. Retina Service.

In the work that followed, Dr. Constable sought the collaboration of Dr. Herman D. Suit, MGH Chief of Radiation Medicine. When Dr. Constable later accepted a full professorship at a university in Australia, Dr. Gragoudas took over the work, continuing the affiliation with the MGH.

Gradually the studies changed direction, from a concept of treating infants with retinoblastomas to the care of adults with malignant melanomas.

The reason, Dr. Regan said, was that proton beam treatments in infants with a retinoblastoma would require general anesthesia which is not possible at the cyclotron facility.

Besides, being relatively radiosensitive, retinoblastomas do yield to other forms of radiation.

Intraocular melanoma patients have come from many parts of the world to receive proton beam treatments offered only by the M.E.E.I.–MGH team. At Berkeley, Calif., the Lawrence Berkeley Laboratories conducts a similar program but uses helium ions instead of protons.

Dr. Evangelos Gragoudas of the Massachusetts Eye and Ear Infirmary retracts a patient's eyelid to keep it away from proton radiation.

Dr. Gragoudas, an Associate Professor of Ophthalmology at Harvard Medical School, said proton beam patients suffer less spread of tumor cells than patients who undergo eye removal.

Dr. Suit, who is Professor of Radiation Therapy at Harvard Medical School, sees far-reaching uses for the proton beam. An author of 18 published scientific articles on the subject, he remarked:

"We've also had impressive successes with proton beams in treating sarcomas at the base of the skull which impinge on or abut critical structures of the central nervous system."

He said he and other investigators are intensively evaluating proton beam radiation as a tool to combat cancers at other sites.

For example, Dr. Suit said, several patients with abdominal tumors have received the treatments with hardly any symptomatic reactions.

"These patients would have been quite sick for a while if conventional techniques had been used," he declared. "But with the proton beam, we were able to put the radiation right where the tumor was. We didn't have to irradiate any uninvolved intestinal tissue." ■

When the Body's Filtering System Fails

(First of two articles)

Food is the basis of life, giving the body nourishment for proper growth, strength, and well-being.

Yet every food (even that "perfect" one called mother's milk) contains some ingredients which have no value and must be discarded.

Among the body's chief organs for eliminating waste are two fist-sized kidneys situated on either side of the spine at the small of the back.

Containing 140 miles of tubes and filters (glomeruli), the bean-shaped kidneys can function to a degree far beyond normal requirements. In fact, one kidney can do the work of two without undue strain; hence, the thousands of people who live normal lives after removal of a kidney.

Weighing only five ounces each, the kidneys filter the body's entire blood supply 40 times a day, disposing of chemical wastes and excess fluids through the bladder in the form of urine.

Maintaining a healthy environment for cells constitutes only one responsibility of the kidneys. They also modulate certain activities in the body.

The kidneys produce an enzyme called renin which affects blood pressure by controlling another chemical agent, an artery-constricting hormone called angiotensin (*MGH News,* December 1976–January 1977). Through manipulation of angiotensin, the kidneys also indirectly control the body's salt and water balance.

The kidneys produce a hormone (erythropoietin) which determines the number of circulating red blood cells. And the kidneys turn vitamin D into a hormone to regulate the absorption of calcium from the gastrointestinal tract.

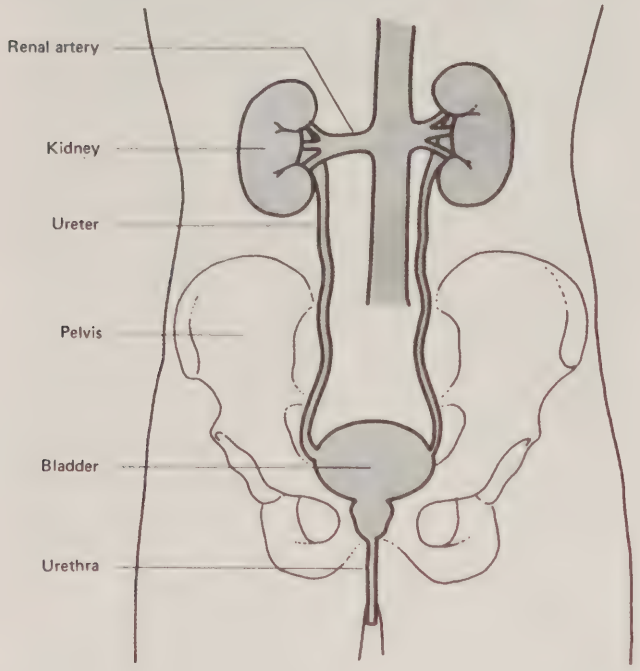
The importance to life of the kidneys may explain why everybody is born with two of them. Even with two, however, crises can and do arise.

Disease may be present in one or both organs long before any symptoms appear. With some two million functioning units (nephrons), the kidneys can perform their tasks without impairment to health until only 10 or 20 percent of the units remain undamaged. Beyond that the excretion of waste products becomes less efficient, and the first signs of illness surface.

Even then the symptoms may be nonspecific: loss of appetite, some nausea, fatigue due to development of anemia, shortness of breath, and increased frequency of urination, especially at night. If the patient has high blood pressure, the kidney condition may affect vision.

(Continued on Page 6)

An Ailing Kidney Often Recovers



Drawing illustrates how urine leaves the body after excretion by the kidneys.

(Continued from Page 5)

"Regardless of what disease has impaired the kidneys, the presentation of symptoms will generally be the same," said Dr. Alexander Leaf, Chief of the MGH Renal Unit. "The symptoms simply reflect a reduction in the mass of functioning kidney tissue."

Diseases of the kidneys affect more than 13 million Americans. Most live a relatively normal existence, but each year as many as 17,000 people fall into what doctors refer to as end-stage, chronic renal failure. For them drastic measures must be undertaken to prevent death from accumulation of wastes in the blood (uremic poisoning).

The treatment usually includes a cleansing of blood three times a week by a process called hemodialysis. This government-funded program involves hooking the patient to a complex machine for several hours at a time.

An alternative, more recently developed method of extracting toxic substances from blood is finding increasing favor. Called peritoneal dialysis, the treatment involves use of the peritoneum, the lining of the abdominal cavity, as a natural filter.

The cavity is filled with a special solution. Then, waste materials pass through the lining into the solution. The fluid is replaced several times a day.

Although peritoneal dialysis allows the patient freedom of movement, physicians exercise great caution in selecting candidates for this technique. Failure of the patient to remain on guard against infection could invite peritonitis, a potentially fatal inflammation of the abdominal lining.

In a hospital, the risk of peritoneal dialysis is minimized because the patient remains in a sterile or near-sterile environment until he is better.

While hemodialysis and peritoneal dialysis are mainstays for the chronic kidney patient, doctors frequently turn to these procedures as stopgap measures in treating the acute patient.

Dr. Leaf said he and colleagues in the Renal Unit, which he founded more than 25 years ago, prefer to dialyze by the peritoneal method if the rate of tissue breakdown is high and much waste has accumulated. "We would dialyze the acute patients almost around the clock for three, four, or even five days," he said.

Acute kidney failure generally is self-limited; that is, with proper attention, a malfunctioning kidney most often will return to normal in due time. The kidney has remarkable regenerative capabilities.

Dr. Leaf said acute kidney conditions encountered at the MGH cover a broad spectrum, but the most common comes from an insufficient blood supply to the organ.

This could stem from shock, a collapse of blood circulation marked particularly by a drop in arterial blood pressure; failure of the heart and lungs, or even prolonged surgery.

"If the blood supply to the kidneys halted for only a brief period, say 30 minutes, the organs would function again on resumption of the circulation," Dr. Leaf said. "But if the kidneys were obstructed for a longer time, an hour or more, the physicians would have to cope in almost all instances with an acute ischemic renal failure [a kidney failure resulting from tissues being deprived of blood]."

Anywhere from 3 days to 3 weeks may pass during which the kidneys will be unable to function normally, but the special care that can be given in a hospital can tide the patient over until the ailing kidneys recover.

Most of the waste products that the kidneys have to excrete, such as urea, phosphorus, creatinine, and organic acids, come from end products of protein digestion. "So we try," said Dr. Leaf, "to suppress protein breakdown as much as possible.

"We can do this by giving the individual pure sugar or pure fat. This would satisfy the patient's caloric requirements and reduce the rate at which he breaks down tissue.

"If the patient had a fever, which would accelerate tissue impairment, we would treat the fever with antibiotics. If the patient lost too much water through the skin and became dehydrated, we could administer the needed volume of fluid to keep the kidneys adequately perfused [bathed in liquid]."

When these simple measures fail to reduce the waste products sufficiently, doctors might resort to dialysis.

In addition to interruption of blood flow, acute kidney failure can follow ingestion of any one of a number of toxins encountered in the environment, such as lead and other heavy metals.

Sometimes procedures aimed at helping a patient can themselves harm the kidneys. Yet in a hospital treating desperately ill patients or those with complex difficulties, more aggressive diagnosis and treatment are necessary to save lives. Physicians have to balance the risk of doing a procedure against the risk of not doing it.

Thus, doctors at the hospital routinely check the creatinine level in patients scheduled for blood vessel X rays (angiography). Since this procedure entails the use of contrast material which must later be excreted by the kidneys, a high level of creatinine coupled with a high concentration of contrast media could cause the kidneys to falter.

"Some of the stronger antibiotics, essential for treating infection, also can put a patient at risk for developing kid-

Helping the Constantly Restless Child

The two 7-year-olds seemed like bundles of energy as they mixed it up with several chums in a game at a neighborhood park. By their hard blocking and tackling, Jimmy and Tommy had clearly forgotten that they were supposed to be playing touch football.

The two long-time pals often were termed "two peas in a pod," but nothing could have been further from the truth.

Following vigorous late afternoon exercise, for example, Jimmy would go home, clean up, sit down to dinner, work on a model plane he was building, and then go to sleep to be rested for school the next day.

In Tommy's home, the scenario differed. On returning from play, he often remained rambunctious. Throughout his meals he fidgeted. Later, he would try to occupy himself with some diversion, but nothing held his attention for long. Finally, he would go to bed, hating the thought that in only a few hours he would have to go to school again.

At play, Jimmy and Tommy indeed were much alike. But although seemingly charged up at times, Jimmy could later settle down and function according to the occasion. Tommy could not. At school, home, or playground, he exhibited an unending restlessness.

His condition bears several labels: minimal brain dysfunction, hyperkinesis, hyperactivity, and attention deficit disorder (A.D.D.). Many parents would simply describe the child as "impossible."

"This is a complex condition that physicians and others are only beginning to really understand," said Dr. Michael S. Jellinek, Chief of the MGH Child Psychiatry Service.

"It is a major disorder and a many faceted one. Hyperactivity may be just one component, or, in some children it may not even be present. We think the newest name, attention deficit disorder, fits best."

Dr. Jellinek said A.D.D. might involve several symptoms such as hyperactivity, a tendency to act impulsively, a short attention span, and even learning disabilities.

He compared the current understanding of A.D.D. to the status of pneumonia some years ago. Doctors detected pneumonia by listening to the lungs with a stethoscope or by studying a chest X ray. Then they prescribed treatment. Today, before deciding on treatment, they must determine what form of pneumonia is present. Bacterial? Fungal? Viral?

"Attention deficit disorder is at the phase," said Dr. Jellinek, "where it has been reasonably defined and where people can begin to study its subtypes to see whether an improved treatment approach is possible."

It is very easy, he said, to misdiagnose A.D.D. in a child who is anxious, simply overactive, or unable to learn quickly. But he went on:

"If one obtains a careful history of the patient, confers with his parents and teacher, observes and talks to the child, and then analyzes all of the information, one can make an accurate diagnosis."

Signs of the disorder usually become very evident soon after enrollment in school because, as Dr. Jellinek put it, "if a child cannot pay attention and concentrate on tasks in class, that is where the 'real world' will catch up to him."

A subsequent look at the patient's history often reveals evidence of the affliction as early as age 3 or 4.

Start of the condition at an early age and prevalence in a variety of settings, i.e. home, school, play, are important clues to A.D.D. For some unknown reason, it affects more males than females; the ratio has been estimated as high as 10 to 1.

What causes the child's problems? No one knows for sure, but some physicians suggest that A.D.D. may result from an immature nervous system.

The theory of a developmental delay may be supported by the fact that some A.D.D. children either outgrow their difficulties or in certain ways manage to compensate over the years for the shortcomings.

Some investigators are checking whether various food additives can intensify problems of concentration and control of motor activity in an A.D.D. child.

Dr. Jellinek said, however, that while looking into the effect of foods may be worthwhile, the study results

(Concluded on Page 8)

---

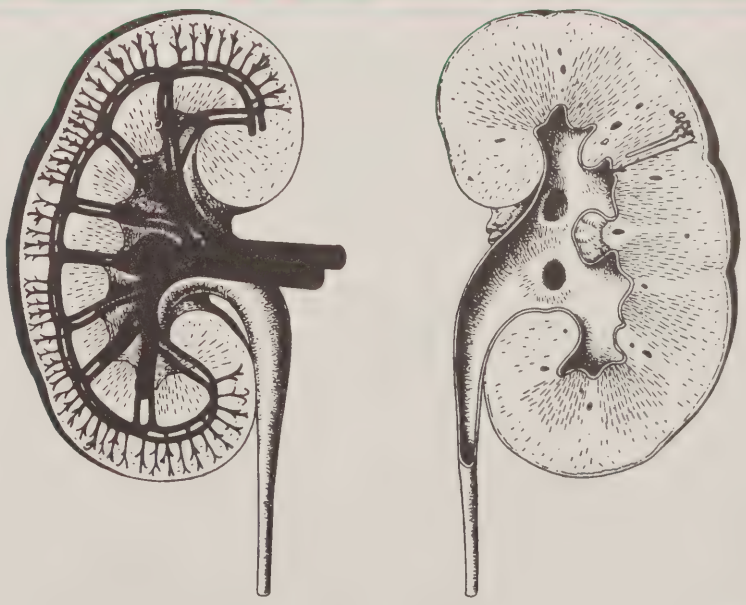
ney problems," said Dr. Leaf, who is also Chairman of the Department of Preventive Medicine and Clinical Epidemiology at Harvard Medical School.

"Doctors try to use these drugs cautiously, but despite the greatest care, patients vary in their susceptibility to kidney damage, and it may be very difficult for doctors to predict who is at risk."

Still another cause of kidney trouble is an enlarged prostate gland. Usually affecting men in their middle or later years, the enlarged gland obstructs the urethra, the canal which carries urine from the bladder. The urine then backs up into the kidneys.

Removal of the prostate gland for this and other reasons is one of the most common operations performed by urologists. ■

(Next: The Chronic Kidney Patient)



Two views of a kidney's internal structure; at left, depicting circulation in the organ and, at right, showing its hollow funnel (or pelvis) and the ureter into which urine empties.

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Child With Attention Lag Needs Tolerance

(Concluded from Page 7)

thus far are very preliminary. Therefore, diet is often not of prime concern at this time in formulating a care plan.

Treatment is a long-term process requiring a team effort, the doctor said. Since A.D.D. persists around the clock, the affected child must have the sympathy, patience, and support of not only the family doctor (and sometimes a medical specialist such as a psychiatrist or neurologist) but also all others who guide him in life.

Once all care givers recognize and understand the limits governing the youngster's behavior and performance, realistic achievement goals can be set for him.

At home, for example, instead of a mother telling her child to "pick up your room," she might say initially, "Pick up these toys." Once done, she could offer a few words of praise and then instruct further.

"The point is that the child might be unable to concentrate on work continuously for 20 minutes but could tolerate 4, 5-minute bursts," explained Dr. Jellinek, who is also Assistant Professor of Psychiatry (Pediatrics) at Harvard Medical School.

Such a patient attitude on the part of a parent, or a teacher in school, could turn a child's feeling of frustration and failure into one of accomplishment and self-worth. Gradually he could be given more important and more difficult tasks.

Sometimes physicians find stimulant drugs useful in treating an A.D.D. patient. Stimulants for a child who is already hyperactive? Actually drugs, such as methylphenidate, pemoline, and amphetamines, enable the patient to concentrate better, and thus he becomes less agitated and less of a discipline problem. But he does not necessarily learn more easily.

Studies are under way at some centers to determine whether changes in doses might improve learning potential while at the same time controlling behavior.

At the MGH, Dr. Joseph Biederman, Director of the Pediatric Psychopharmacology Clinic, hopes to launch studies soon to learn whether other drugs can help the A.D.D. child.

"Inasmuch as attention deficit disorder embraces various types of problems, a particular medication might help one child, but not another," said Dr. Biederman. "We think it is very important to see just what options we might have in treating these conditions.

"Also much of the medicine we now use for A.D.D. is short-acting. After three or four hours, the effect wears off. If a child is very hyperactive or has frequent temper tantrums, the situation can become very difficult for the family."

Dr. Biederman thinks certain antidepressants might be one solution. Found to have a similar effect on A.D.D. patients as stimulants, the antidepressants need to be taken only once or twice a day to be fully effective.

Whatever the form of treatment, Dr. Jellinek advises an early start because poor achievement gives a child a poor self-image, and demands for achievement accelerate in higher school grades.

"This can create a snowballing effect of falling farther and farther behind," the doctor pointed out. "When a youngster is scolded and thinks everything was his fault, it is not difficult to imagine him wanting to skip school and even entering into delinquent kinds of activities."

But even if a child does poorly in school, with proper counseling he may grow up to be a happy and successful adult.

"School points up deficiencies, while there are compensations in the 'real world,'" Dr. Jellinek said. "One can be an astute businessman and a lousy speller, but society won't complain about the spelling." ■

While a hyperactive child may seem no different from a boisterous but normal youngster during play, symptoms of the disorder continue at home and school.

MGH News

Vol. 41 No. 3 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS April, 1982

Open Adoptions: A Unique Program of Child Care

Seeking the Cause Of Some Chronic Kidney Diseases

(Second of two articles)

"The disease just sneaked up. The patient never had an inkling of anything physically wrong. Yet she had chronic kidney failure. Both of her kidneys had shrunk to a third of their normal size."

Dr. Cecil H. Coggins, Clinical Director of the MGH Renal Unit, was speaking of a 19-year-old woman from Guayaquil, Ecuador. She underwent a routine physical examination in her home city after applying for a job, and blood tests uncovered the advanced kidney disease.

The remarkable ability of these waste-disposal organs to undertake burdens far beyond normal accounted for the woman's false sense of well-being.

Because doctors in Guayaquil could do little for her, she thought of coming to the MGH. She had relatives with whom she could stay in Boston.

Dr. Coggins said her illness has not yet reached the point where side effects such as high blood pressure or bone disease have set in. Thus, appropriate treatment can be started to avoid these potentially damaging conditions. And if doctors can determine the cause of her illness, they may be able to reverse it.

A number of years may pass before the young patient reaches so-called end-stage renal failure when the function of her kidneys must be taken over by blood-cleansing dialysis treatments or by a kidney transplanted from a donor.

Last year, the United States government spent more than $1 billion for the treatment of 40,000 people with end-stage renal disease. That is more than $25,000 per person per year! By 1984 the cost is expected to triple.

Medical investigators are striving to learn more about the natural history of various kidney afflictions. Nearly a third of patients who receive dialysis or a kidney transplant have illnesses of unknown origin.

Dr. Coggins heads a five-year, 17-center project studying a common group of kidney diseases known collectively as chronic glomerulonephritis. Progressing slowly but steadily, the disorders damage the head ends (glomeruli) of a kidney's filters (nephrons) which separate waste materials from blood. The damage results in a serious

(Continued on Page 4)

A year after receiving a kidney transplant, 18-month-old Melissa Saunders of South Hamilton, Mass., clearly is doing just fine.

Adoption is a subject that arouses the emotions of people, emotions often difficult to express.

While bringing joy to couples who might otherwise not have children, adoption also saddens others, the natural parents who surrender a part of themselves.

And there is the child — the often curious child.

Even when adopted in infancy, a youngster may later inquire, "Where did I come from?" Adopted at an older age, children may have vague recollections of their biological parents. For such boys and girls curiosity intensifies.

Historically, society has shrouded adoption data in secrecy while paying little regard to the child's craving to know about his background.

A shift in public attitude now seems in the making. Those who deal with adoptions are opening their minds on the subject. For at least some children, they think, it might be healthy to raise the curtain.

"Many states including Massachusetts are trying out 'open adoption' programs," said Dr. Steven L. Nickman, an MGH child psychiatrist. "In certain situations, the natural mother or father is allowed access to the home of an adopted child, usually a youngster who is at least 6 years old.

"Although still very much an experiment, the program seems to offer a solution to the complex human problems that adoption presents. Many adoptive families find they can live with this compromise arrangement."

A number of populations in Africa and on islands in the Pacific have long

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
Joseph B. Martin, MD, *Interim General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIAL:

Why an MGH Institute?

These are perilous times for institutions of higher learning. Even the more established universities are plunging into treacherous economic waters. Annual costs are soaring well above the $10,000 a year mark even at heavily endowed colleges. Unless they can win scholarships, the middle- and lower-income students are being priced out of college.

So why is the MGH Institute of Health Professions phasing into existence now of all times? As this issue reports, the idea of the Institute was proposed by one former MGH General Director, Dr. John H. Knowles (*MGH News,* February 1971), and made a reality by another, Dr. Charles A. Sanders.

In 1873, the year to which the MGH School of Nursing can trace its origin, college degrees for nursing did not exist. In recent years, though, diploma schools have disappeared just as fast as degree programs have come into being. The value of the old diploma to a starting nurse has tumbled. In this nation of college graduates, the certificates and diplomas of other allied health programs have also deflated in worth. Thus the MGH Institute arrived none too soon. Its ability to replace existing programs with degree-granting ones and to utilize extant campus structures has made the operation an economically spare entity. Fortunately so. For the hard times referred to above would sink a less frugal effort.

Even so the Institute is struggling to find support. The generous fellowship money already donated is an important start. But endowment must be found to finance the academic lifeline of the Institute. The need is great.

Adoptive Parents Must Understand Child's Curiosity

(Continued from Page 1)

followed this policy, but because of America's customs the program is not always practical or acceptable in this country, said Dr. Nickman, who counsels both adopted children and adoptive parents in the MGH Child Psychiatry Clinic. He also leads group sessions involving adoptive parents.

While some studies indicate adoptees are no different from their peers, many workers in child health believe adoption can produce problems.

These problems, they say, may show up in the child in the form of impulsive behavior, difficulty in sticking to a task, feelings of social or personal inferiority, heightened adolescent rebellion, and at times a failure to fulfill early promise.

It is felt that these traits may, in part, reflect difficulties in the child's development of a sense of personal identity and continuity with the past.

Dr. Nickman said that adoptive parents sometimes are at a loss to know how to deal with these developmental setbacks when they arise.

And they apparently arise more often than most people believe.

"As a child psychiatrist and before that as a pediatrician, I've seen many adopted children," Dr. Nickman declared, "and I realized that more adopted youngsters were coming in than would be represented in the proportion of adoptees in the population."

Although 1 in every 100 American children is adopted by nonrelatives, and another 1 percent lives with relatives other than parents, Dr. Nickman discovered in the medical literature that as many as 13 percent of children treated by child psychiatrists are adopted.

"It certainly causes one to wonder whether something about adopted children makes them more vulnerable than other children," he said.

Some observers have said that the time when an adopted child begins to show a difference from others is right after he learns of the adoption.

"It is very important for adoptive

Photographs: Page 1, courtesy of Dr. John Herrin; pp. 4, 5 (lower), 6, 7, Myron Daniels; p. 5 (upper) Don Robinson; p. 8, Scott Davis.

Drawing: Page 3, MGH Medical Art Department.

parents to allow their child to talk about his feelings," the doctor stated. "Letting him express his curiosity and sadness about his natural parents promotes the growth of the child. Denial would tend to hold him back."

Sometimes, recognizing the natural curiosity of an adopted boy or girl, diligent social workers will compile scrapbooks preserving joyful memories of places where the child previously lived. These scrapbooks would accompany the youngster as he moved on.

Dr. Nickman, who is also Instructor in Psychiatry at Harvard Medical School, said some health professionals have urged waiting until a child is 5, 6, or 7 years old, perhaps even older, before revealing that he is adopted.

"Often as soon as a child knows there was another set of parents, he begins to fantasize about what they were like," Dr. Nickman said. "But after age 5 most children fantasize about many things.

"I believe the adopted child can use his fantasy to work out his thoughts about his original parents as well as whatever sadness he might have about not being with the ones who brought him into the world."

Curiosity over one's natural parents can sometimes drive an adopted child to search for them upon reaching maturity. Ten or fifteen years ago, adopted persons who wanted to search were thought to be neurotic. Today, the feeling is growing that this need some adoptees have is a legitimate one.

Dr. Nickman said people who feel they benefited from searching for their parents far outnumber those who now wish they had not. Even though many searches end in sadness — people finding parents who were not interested in them or who turned out to be chronic mental patients — some of these adoptees insist they are glad they at least know something of their past.

Do children ever find their biological parents and wish to be back with them?

"In my experience, that almost never happens," said Dr. Nickman. "The motivation to search is usually one of curiosity about one's origins rather than a dissatisfaction with the home in which the individual is growing up.

"Often, children in adoptive families have felt their parents would be terribly hurt by a search for the original father and mother. Adoptive parents in fact have become less defensive about this. They now seem more able to let their children do what they need to do to satisfy their own curiosity."

Sometimes friction that strains the bond between an adopted child and his new parents stems from the parents' own feelings about the arrangement.

Most adoptions occur after couples discover they are infertile. Unless they make peace with this knowledge, they may wonder when the adopted child arrives whether he will fit in and whether he resembles anyone in the new family. Also, the older the arrival the more the bond between the child and his parents will be at risk.

Adoptive parents can also have fantasies about the origins of their child. Dr. Nickman told of a couple who brought their adopted youngster to him for treatment. The child, in early adolescence, repeatedly acted out, according to the parents, and "has never been like our other children."

It turned out that the couple had always been plagued by a fear that the child might have inherited some antisocial traits from his original parents. The adoptive parents had failed to allow for the normal aggressiveness of a child growing up.

Their attitude worsened the child's tendency to act out so that in some respects he really was becoming antisocial. Unchecked, the disruption to the family could have led to the adoptee eventually leaving the home.

Does society in general harbor any prejudice about adoption?

Dr. Nickman told of a medical colleague who was hurt over the will of a relative who had died. The will left bequests to all children in the extended family except two, those of the doctor-friend. They were the only children who had been adopted.

In facing problems relating to attitudes of parents, children, or society in general, adoptive families have support groups or individuals trained to help: community mental health centers, hospital child psychiatry clinics, and many professionals working in the private sector. ■

Many Clues to Chronic Kidney Ailments

Odete Carreiro of Portugal catches up on the news while undergoing blood-cleansing hemodialysis.

(Continued from Page 1)

leakage of protein from the blood into urine (proteinuria).

By closely following such patients, the researchers can observe the course of the disorders and the patterns of test results. Proposed new treatments may emerge followed by trials under the $1 million program funded by the National Institutes of Health.

Just as prevalent as chronic glomerulonephritis is an array of conditions called chronic interstitial nephritis. They occur between the nephrons in the kidneys, causing some inflammation and fibrous scarring.

"These patients usually don't have proteinuria," Dr. Coggins said, "and that means the condition is harder to detect. A urinalysis at a doctor's office might not even prove abnormal."

Whereas the cause of glomerulonephritis often has an immunologic basis, Dr. Coggins described the interstitial maladies as a big hodgepodge of illnesses, a number of them poorly understood. They could be produced by many kinds of toxins and even by long-term overuse of certain medications such as headache or backache pills containing phenacetin.

Determining whether a patient's kidney disease is chronic (unrelenting) or acute (sudden, but self-limiting) is not difficult. Length of illness offers the major clue, but frequently the chronic patient also presents certain outward characteristics.

He is likely to be pale from anemia; thin because of loss of appetite, nausea, and vomiting; and dry-skinned.

In addition, he may exhibit deep breathing, a twitching of extremities, and itching.

Sometimes the chronic patient is born with a kidney abnormality. It may be a structural defect in the formation of the nephrons (for example, a polycystic kidney) or an obstruction of a ureter, the tube which carries urine from the kidney to the bladder.

Dr. Nina Rubin, Director of the Hemodialysis Unit at the MGH, said that how soon a patient begins dialysis often depends on when the patient becomes symptomatic rather than on the results of kidney function tests alone.

"Dialysis is a total intrusion upon one's life-style," she said. "Therefore, unless some critical event such as fluid overload or high potassium requires our intervention, we wait until the patient himself realizes that he will feel better with the support of dialysis."

Dialysis takes two forms: hemodialysis, involving a four- to five-hour hookup three days a week to a blood-cleansing machine, and peritoneal dialysis, which uses the lining, or peritoneum, of the body's abdominal cavity as a filter.

An elderly patient who cannot tolerate the shifting of a large volume of blood outside the body may do better on peritoneal dialysis. Waste products would be collected in a special solution placed in the abdomen and changed periodically.

Dr. Rubin stressed the importance of input by several specialties in caring for a patient stricken with end-stage kidney disease. The internist or nephrologist who prescribes treatment relies on contributions by people in dietary, social service, psychiatry, and nursing; also pediatrics, if a child is involved. Together, these specialists help the patient and the family to cope.

Diet, for example, is critical. The chronic patient must cut down on meats because his kidneys cannot process a normal protein load. If he cannot excrete potassium properly, foods such as chocolate, bananas, and grapefruit must be pushed aside. High blood pressure? Shun the salt.

Dr. Rubin's unit provides an environment like intensive care for the MGH's medical, pediatric, and surgical service patients who suffer from renal failure. Children represent more than 30 percent of the patients in the unit.

Dr. John T. Herrin, Chief of Pediatric Nephrology, cares for the children. He describes their diet as particularly vital to their well-being because, unlike adults, youngsters are still growing. Striking a balance between needed food intake and food restrictions can be difficult.

Since convincing children of the need for a proper diet is also difficult, Dr. Herrin feels they should be dialyzed or given a functioning kidney as early as possible. Such support often enables the doctor to relax the diet.

Children, he said, seem to tolerate both hemodialysis and peritoneal dialysis quite well. They understand the limits placed on their activities and manage their new life-style as easily as their adult counterparts.

Much of the credit goes to the team assistance which allows the child to maintain as normal a routine as possible at school and play while continuing to receive necessary medical treatment.

Occasionally a patient on hemodialysis can run into a problem. The treatment requires that the individual receive heparin, an anticoagulant drug, to assure that his blood will not clot in the dialyzing equipment. If a patient tends to bleed easily or has just had major surgery, heparin could accentuate problems.

Dr. Rubin; her husband, Dr. Robert H. Rubin of the MGH Infectious Disease Unit; and Dr. Randall M. Zusman, of the hospital's Cardiac Unit, have been working to overcome the clotting threat.

Reporting in the *New England Journal of Medicine,* the investigators described how they successfully dialyzed

How Some Illnesses Can Spark a Fever

High among man's attributes is his body's ability to adjust to environmental change.

While cold-blooded creatures such as fish, frogs, and snakes have a body temperature which must coincide with that of their surroundings, the temperature of man remains constant regardless of the weather. Thus his domain is boundless.

The advantage enjoyed by man stems from an ability to maintain a delicate balance between his body's heat production and its heat loss.

Although the thermoregulatory center in the brain is wonderfully efficient, the built-in thermostat often can be thrown off when illness strikes.

Many types of inflammation and infection can cause the thermostat to reset upward. They delude the brain into thinking that the body's normal reading of 98.6 °F is, for example, 95 °F.

The height of a fever is often age-related.

The outside of the body begins to feel cold as blood vessels in the skin constrict and heat gravitates to deeper, more critical areas of the body. Subsequently, in response to a shaking chill which generates more heat through muscle activity, the brain allows the patient's temperature to rise a few degrees to what the brain thinks is a normal level. The net effect is a fever.

Usually fever will persist until the infection or inflammation resolves itself, or a counteracting drug is taken.

To lower the temperature, the body dilates blood vessels in the skin (causing flushing) and also produces sweat which upon evaporation induces a cooling effect.

Temperature rises by a common pathway. The illness, whatever it may be, stimulates the release of a substance called endogenous pyrogen from the walls of white blood cells. The pyrogen then travels to the brain's hypothalamus, seat of the thermoregulatory apparatus, and proceeds to alter the temperature setting.

Aspirin can both restore the normal

(Continued on Page 6)

some very ill patients by using a natural body substance called prostacyclin instead of heparin. Prostacyclin inhibits clotting by preventing blood platelets from collecting and by keeping blood vessels expanded (*MGH News,* December 1981). Its effects can also be turned on and off more readily than those of heparin.

When patients undergo a successful kidney transplantation, their need for further dialysis ends. At the same time, however, patients gain comfort from knowing that if their donated kidneys ever fail dialysis remains available as a life-saving procedure.

Since the early 1960s the MGH has performed more than 450 kidney transplantations, and they are continuing at a rate of 45 to 50 a year.

Dr. A. Benedict Cosimi, Chief of Clinical Transplantation Surgery at the MGH, said that about 80 percent of kidneys donated to patients at the hospital by relatives have survived at least one year. For organs donated from cadavers, the one-year survival rate, he said, is 60 or 65 percent at the MGH, somewhat higher than the national average. Survival of patients is much higher than that of donated kidneys because after rejection of a transplanted kidney the patient can return to dialysis until another donor is found.

Studies show a three percent loss per year after the first year for organs of living related donors and a six percent loss annually after the first year for organs from cadaver donors.

A new biological tool called a "monoclonal antibody" is proving very efficient both in monitoring kidney recipients for early signs of transplant rejection or infection and in treating patients after rejection has already begun.

Made in a laboratory, these monoclonal, or isolated, antibodies are able to zero in on white blood cells known as "T-lymphocytes" which play a major role in the body's natural attempt to turn away foreign tissue.

Dr. Cosimi and his team are trying to develop a protocol of treatment with monoclonal antibodies that would attack only the specific type of T-lymphocytes that reject kidneys.

Even as Dr. Cosimi and his colleagues move forward in this field, they report another promising development in efforts to protect kidney transplants.

The group is studying in animals a drug called Cyclosporin-A, which appears to preferentially suppress the specific type of T-lymphocytes rejecting kidney grafts. Some medical centers elsewhere already are using Cyclosporin-A with patients.

Dr. Cosimi, like his medical colleagues a member of the Harvard Medical School faculty, sees great hope in the developments:

"We're embarking upon new forms of suppression which promise to be much more selective, and therefore should make transplantations possible for many more patients who either suffered rejection previously or were unable to obtain a kidney at all." ■

Kidney recipient Melissa Saunders with her MGH specialist, Dr. John T. Herrin.

A Moderate Fever Often Proves Useful

(Continued from Page 5)

setting and fight inflammation. Acetaminophen, marketed under many brand names, lowers temperature but is not anti-inflammatory. Nonsteroidal anti-inflammatory agents, often prescribed for rheumatoid arthritis, can stop endogenous pyrogen production.

Ironically, other medicines themselves can cause fever. And the temperature patterns may vary widely among patients taking the medications for one illness or another. Generally, the elevated temperature can be reduced within 48 hours by discontinuing the offending agent or by substituting a chemically unrelated medicine with the same capability.

Since fever represents a manifestation of disease rather than the illness itself, physicians often will not prescribe any drugs to bring a moderately elevated temperature down.

The reason is that fever may be useful as an internal barometer of the patient's condition. A temperature reduction could signal that the patient is recovering.

Dr. Newton E. Hyslop, Jr., a member of the MGH Infectious Disease Unit, cautioned that a high temperature requires immediate attention. "Although it is unusual for fever in an adult to get out of control," he said, "people can become irrational at a temperature of 103 °F or higher, thereby creating complications such as delirium." He added that when a temperature rises above 106 °F the brain can suffer permanent injury.

Dr. Hyslop, an Assistant Professor of Medicine at Harvard Medical School, also said that the height of the fever is often age-related.

"Children characteristically overshoot when they have a resetting of their thermostats," he declared. "In a child, for example, a fever of 104 °F or 105 °F might accompany an attack of pneumococcal pneumonia. In the elderly, the same serious illness might generate a fever of only 99 °F."

A high grade fever in a young child could suddenly jump from 103 °F to 106 °F and produce convulsions if steps are not taken quickly to control it, the doctor said. Youngsters do not have a very good control of their heat radiating systems. They may not be able to sweat adequately, for instance.

Infections in children are exceedingly common. Some pediatricians have estimated that during their first decade of life children experience perhaps 10 infections a year, some producing fever.

But youngsters are also quick to develop immunity. Dr. Donald N. Medearis, Jr., Chief of the MGH Children's Service, spoke of a respiratory infection caused by parainfluenza virus-type three.

"Everybody gets it, usually by the age of 3," he said. "The first time the illness hits, the patient gets fever, a cough, and even mild pneumonia. The second time, there is less fever, a cough, and some inflammation in the larynx, windpipe, or bronchial tubes, but no pneumonia. The third time, the patient may just experience a cold."

Dr. Medearis said he thinks it is wrong to administer aspirin or acetaminophen to a sick child on a routine basis, such as every four or six hours for the next several days. Instead parents should be advised to give a certain amount of the medication to the child if his temperature becomes high and then see what happens. If the temperature rises again and the child remains uncomfortable, the drug may be given again.

A sponge bath can often help to make the young patient more comfortable. Lukewarm water not only has a calming effect on a child, it induces dilation of blood vessels in the skin so that so-called core heat deep in the body can, in effect, radiate to the outside world, in part by the evaporation of the water.

Dr. Medearis, who is Charles Wilder Professor of Pediatrics at Harvard Medical School, warned that cold water or ice water should not be used unless the patient's body was extremely overheated (hyperthermia) and needed very rapid cooling. He said the treatment is very unpleasant for the child and is really an emergency procedure to be given only in a hospital.

One reason why Dr. Medearis urges caution in the use of aspirin and acetaminophen is that they are not only among the most used drugs but also the most abused.

Taken too frequently, aspirin and acetaminophen can have a cumulative effect, causing a child to suffer nausea and vomiting. In sufficent quantity, these drugs can cause death.

Dr. James M. Easom, Assistant Director of the Massachusetts Poison Control System, said that although frequency of ingestion remains an ever present threat, child-resistant caps and limiting the number of aspirins per bottle help to protect against overdoses in children.

In discussing fever, one cannot overlook an exceedingly rare and apparently hereditary fever that physicians dread. The condition is called malignant hyperthermia (*MGH News,* April 1976).

This can occur occasionally in the operating room when the patient is anesthetized. The individual's temperature can suddenly soar to 108 °, sometimes even higher, and it is vital that the physicians react immediately to

Dr. Donald Medearis, Chief of the Children's Service, visits Neonatal Intensive Care Unit where incubators assure a proper temperature environment for infants whose bodies cannot adequately regulate their own warmth.

New MGH Institute Fashions Advanced Programs of Study

Last May 29 the 108-year-old MGH School of Nursing, the third oldest in the United States, graduated its final diploma class and headed in a new direction.

The school became part of the degree-granting MGH Institute of Health Professions. Established without fanfare in 1980 on the hospital campus, the Institute is gearing to ensure continued leadership in several vital areas of health care.

After awarding diplomas to nearly 8,000 young men and women, the School of Nursing found that its long tradition of excellence was not enough to satisfy the demands of today's society.

Standards for comparing educational achievements had changed and now were based on progress at the university level. A system of credits to evaluate what one has learned is regarded as a basic necessity today.

Julian F. Haynes, Ph.D., the Institute's Provost, said the American Nurses' Association feels that the baccalaureate level should be the minimal entry point for someone seeking to become a registered nurse, and this stand is coming to be widely accepted.

At the end of its first five years of operation, the Institute expects that nursing students will comprise some 60 percent of its enrollment. But the machinery for launching the new nursing program envisioned by the Institute grinds slowly and carefully.

Plans call for a three-year program leading to a Master of Science in Nursing degree for students who already have earned nonnurse baccalaureate degrees.

Dr. Julian Haynes, Provost of the MGH Institute, and his assistant, Mrs. Cynthia Snow, supervised renovation of Bartlett Hall to house offices for the Institute's faculty.

Dr. Haynes said, "We already have applications for the first classes in nursing, but we can't admit anybody until we have a formal go-ahead from the Massachusetts Board of Registration in Nursing."

That approval is expected in time to begin classes next fall. Of more than 100 applicants, about 30 would be enrolled.

In embracing both general and specialized courses in its master's program in nursing, the Institute has planned the equivalent of a 2½-semester school year, rather than the customary 2 terms.

"Three or four similar programs are in operation around the country, including one at Yale," Dr. Haynes said, "and they are well received."

As the Institute irons out details for nurses' education, it is moving ahead in other areas of specialization.

When the school opened in the fall of 1980, it admitted four full-time students in a one-year course leading to a Certificate of Graduate Study in Social Work in Health Care. The current class has a dozen students. The next will have about 20.

A two-year master's program in physical therapy also began in 1980 with an enrollment of four students. The entrance requirements include a bachelor's degree, registration as a physical therapist, and at least two years of practical experience in the field.

Last year, the Institute launched a one-year Graduate Program in Dietetics, accepting four students who already had bachelor's degrees in that specialty and were practicing registered dietitians.

A second type of program in this

(Concluded on Page 8)

prevent the attack from being fatal.

In recent years tests have been devised which help to determine in advance of surgery whether a patient is susceptible to malignant hyperthermia. The procedures are usually performed on relatives of a patient suspected of being at risk.

One test at the MGH involves measurement of calcium absorption in muscle tissue with the aid of a radioactive tracer. Snippets of frozen tissue can be shipped to the hospital from anywhere in the country for study.

Another procedure, this one still in the investigational stage, does not involve putting anything into the body. Called a tourniquet test, a band is placed around an upper arm for about 10 minutes. Upon release, a wrist nerve is stimulated electrically, and doctors observe the twitch response of the nearby thumb. An abnormal increase in twitch would indicate someone susceptible to hyperthermia.

Dr. James T. Roberts, an MGH anesthetist who developed the technique with a colleague, Dr. Hassan H. Ali, said studies have shown a better than 80 percent correlation between a positive result in the test and the diagnosis.

Also new in the care of malignant hyperthermia patients is a muscle-relaxing drug called dantrolene. Long used in pill form for certain spastic muscle conditions, dantrolene was approved for intravenous care of hyperthermia patients by the United States Food and Drug Administration at the request of Dr. John F. Ryan, MGH Chief of Pediatric Anesthesia, and others.

Dr. Roberts said that "if we can detect the syndrome early enough, we can stop it with this drug." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

MGH Institute Continues to Take Shape

(Concluded from Page 7)

field, a two-year Combined Dietetic Internship-Graduate Degree Program, will be offered in the fall. Applicants are now being selected.

This internship-graduate study combination which replaces the internship offered by the MGH Department of Dietetics already has received accreditation from The American Dietetic Association.

Still another graduate level course, one leading to a Master of Science in Speech-Language Pathology, is on the drawing boards, along with two programs that would lead to Bachelor of Science degrees in Respiratory Therapy and Radiologic Technology.

The Institute, which has a present enrollment of 52 students, purposely is moving slowly.

"Even though some courses already have begun, we're still in the process of setting up an entirely new Institute," said Dr. Haynes, who previously was Acting Dean of the School of Arts and Sciences at the University of Maine.

"We're in the midst of assembling the governing mechanisms of the Institute and formulating its academic policies."

And he stressed that the process of gaining Institute accreditation from the New England Association of Schools and Colleges takes six years. Most accreditations to be sought by the new school will be contingent upon a formal stamp of acceptance by the New England Association.

As with most new schools of higher learning, the MGH Institute of Health Professions is beginning on a modest footing both financially and physically.

It has nearly $1.2 million to provide financial aid to students who would otherwise be unable to pursue an education in the Institute.

The largest single source of aid is a half-million-dollar student fellowship fund established by the Rockefeller Foundation in memory of its late president, Dr. John H. Knowles, who died in 1979.

Prior to joining the Foundation, Dr. Knowles served at the MGH for 20 years, 10 as General Director. Formation of an Education Division was a dream of his that was later fulfilled by his successor, Dr. Charles A. Sanders.

Recipients of Knowles Memorial Fund Fellowships are chosen nationally on the basis of merit. The aid is intended primarily for minority students, women, and students from developing countries.

Dr. Haynes said the family of Dr. Knowles has privately added enough money to create an extra fellowship. The contribution is in line with the Institute's encouragement of donations of any size.

Most of the Institute's classrooms and teaching laboratories are situated in Ruth Sleeper Hall on the MGH campus. However, Institute students have access to a full range of inpatient and outpatient care facilities both in the hospital's 13-acre complex and in affiliated neighborhood health centers.

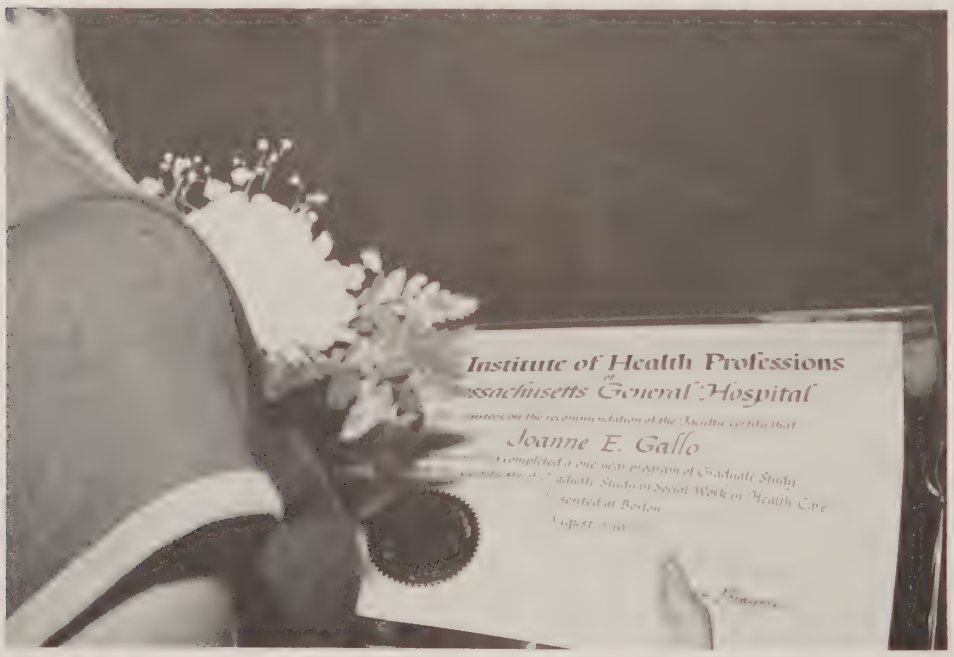
Administrative and faculty offices are situated in Bartlett and Sleeper Halls. Both buildings also house important health science libraries.

Dr. Haynes expects that in five years enrollment will total about 250 students.

Nursing and all other studies being offered are fields in which the MGH has built a reputation for high standards of excellence.

"They're all areas that involve direct patient care, areas in which the hospital has clinical facilities, and areas where there was an interest on the part of clinical units," said Dr. Haynes. "So I really see the Institute as an extension of activities that have always gone on at the MGH.

"In allied health education, I don't think there's anything else in this country which has the breadth of what we're doing here." ■



One of the first graduates of the MGH Institute, Joanne Gallo of Brookline is now a Research Assistant in the hospital's Psychiatry Service.

MGH News

Vol. 41 No. 4 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS May, 1982

Artificial Implants Can Supply Many Real Benefits

Self-Help Groups Provide a Hand In Readjusting

Instinctively when a major health crisis pervades one's life the first question raised is, "Will I survive?"

As the crisis abates and survival is assured, the next question often posed is, "*How* will I survive?"

The patient recovering from a heart attack . . . the woman who underwent a mastectomy . . . the person who must wear a colostomy bag to collect body waste. All may need help to cope.

"People with a medical problem cannot manage without support of the health care system," said Phyllis Silverman, Ph.D., an Assistant Professor of Social Work at the MGH Institute of Health Professions, "but another kind of help they need, help to go on living, may be provided by peers."

In many circumstances, who can respond better than those who have experienced the same crisis, asked the same questions about their future, and found answers that helped.

For an individual trying to recover from a crisis, self-help groups can expand his repertoire of coping strategies so that he will have some sense of how to react to future situations.

Carolyn Tamer, RN, a nurse clinician at the MGH, trains patients in the use of special bags needed for the discharge of body waste after diversionary surgery for cancer or other problems.

Since the operation means a new lifestyle for the patient, Miss Tamer often contacts the Ostomy Association of

(Continued on Page 7)

In trying to improve the quality of life of patients, physicians sometimes must complement ingenuity with creativity.

By teaming up with other specialties, medicine has overcome many challenges once thought insurmountable.

Since the body basically is a machine with parts subject to wear or to destruction by disease or injury, medical scientists and engineering specialists have collaborated to produce a wide array of artificial replacements.

The results often have proved dramatic.

Consider, for example, the plight of a young housewife who was rushed to the MGH as fire ravaged her home. With second- and third-degree burns extending over 80 percent of her body, she lacked enough uninjured skin for doctors to transplant over the wounds.

Metallic hip component (left), developed by Dr. William Harris of MGH, is viewed on X ray later after implantation in patient.

With such an extensive uncovered area, she would probably have died of infection and loss of fluid. But doctors had an option.

They turned to artificial skin developed and used at Massachusetts General Hospital–Shriners Burns Institute and Massachusetts Institute of Technology.

The patient, in her late 30s, received extensive quantities of the man-made, two-layered skin. The bottom (dermal) layer contained a mixture of ingredients from cowhide and shark cartilage. The outer (epidermal) layer consisted of a rubber-like plastic (Silastic).

After about a month, Dr. John F. Burke, Chief of the MGH Burn Unit and of the MGH–Massachusetts Eye and Ear Infirmary Trauma Service, removed the artificial outer epidermal layer and replaced it with healthy, natural outer skin by then available from the patient's body. Slowly the woman improved, one of more than 30 patients to benefit from similar treatment.

Even as she was recovering, Dr. Burke and his codeveloper of the artificial skin, Professor Ioannis V. Yannas of the Department of Mechanical Engineering at M.I.T., reported progress in efforts to make an even better artificial skin.

Called a "stage two" version and used to date only on laboratory rodents, the newest skin can be applied in a single surgical step. Epidermal skin need no longer be transplanted to the wound. And the wait of 30 days or so for the injured area to heal is approximately halved to 14 days or less.

The key to the new version involves

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
Joseph B. Martin, MD, *Interim General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIAL:

A Mere Matter of a Few Billion Neurons

Not too many years ago science fiction created the robot. Today television has its bionic population. Yesterday's science fiction seems more and more like today's reality. One by one the parts of the human body become artificially reproducible: bones, joints, organs, blood vessels, blood, and skin.

Clearly the status of these advances covers the spectrum. Some, like the totally implantable artificial heart, have yet to be used as a permanent replacement for what nature provided. Others like artificial skin are fewer than two years beyond their first trial. And some like artificial heart valves and total hip replacement have been around for a generation.

Are there any parts that defy ultimate replication by man? Had someone asked the question 25 years ago, he would have triggered a long list. Now the list grows short. Many scientists would include the brain.

Like the heart, people tend to endow the brain with mystical qualities. In fact, though, the heart is a relatively simple organ. It is a pump, a marvelously relentless one that sometimes beats for what may be more than 100 years. On the other hand the brain is as complex as the heart is simple. For starters the brain weighs several times more than the heart. An estimated 10 billion neurons, the basic unit of the nervous system, inhabit the nervous system including the brain. While most neurons are tiny, one stretches from the brain to the low back and another from there to the great toe. Some neurons carry information from the rest of the body to the brain. Others relay messages from the brain to muscles. The brain paces our heartbeat and controls our breathing, our appetites, and body temperature; senses differences in texture and weight, makes us aware of sight and sound, able to feel pain, experience pleasure, anger, or anxiety, make decisions, remember and profit from the past, plan for the future, communicate with others, and analyze ourselves.

With all these and other attributes the brain is obviously too sophisticated ever to be artificially replicated. Right? Probably wrong.

Perhaps man will never develop an artificial substitute as sophisticated as the brain. Yet the computer has already made such strides in a few years. Who can say that mankind will never at least approximate artificially many aspects of the human brain.

Implants Demonstrate Value of Teamwork Among Specialties

(Continued from Page 1)

"seeding" the artificial skin with live epidermal cells taken from an uninjured portion of the body. Since the cells are not rejected, they can interact speedily with wound tissue to form functional new skin.

One to three years may elapse before stage two skin becomes available for human trials.

In discussing the skin studies, Dr. Burke stressed that neither team could have succeeded alone. "We needed the engineering know-how that M.I.T. could provide, and they needed our medical expertise," he said. "Miniscule deviations in the pores of the fabricated skin, for example, could have spelled the difference between whether it would work biologically or not."

Dr. Henry J. Mankin, Chief of Orthopaedic Services at the MGH, said that "over the last 25 years or so, implants have tremendously altered our ability to care for patients."

The greatest impact in orthopedics, he said, has come from development of the artificial hip, exquisitely designed internal fixation devices, and instrumentation for straightening the spine.

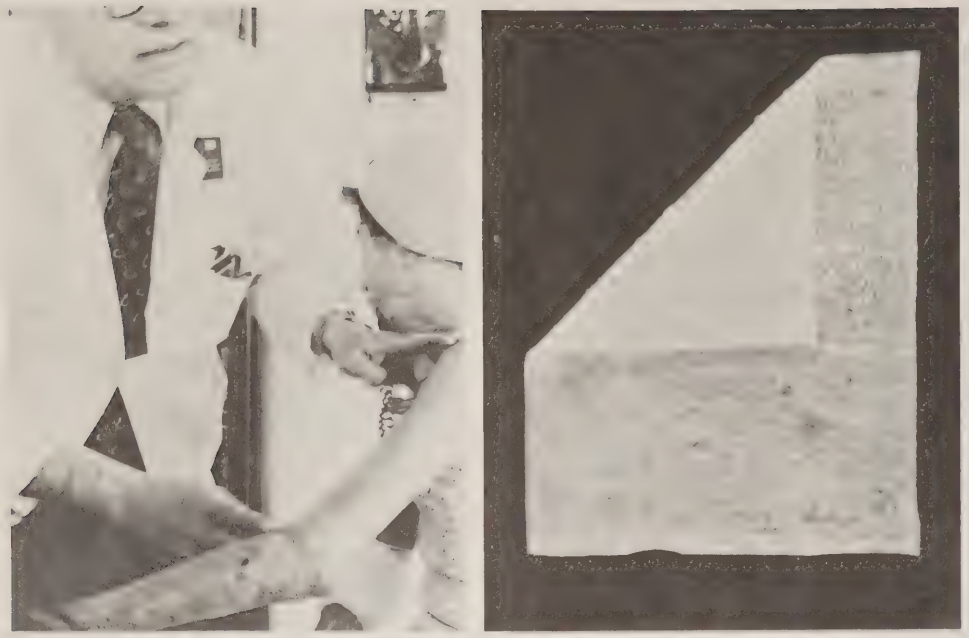
Implants made of stainless steel or a cobalt-chromium alloy are very well tolerated by the body. Surgeons use metallic devices in rebuilding many joints, in holding segments of bone together until healing occurs, and in strengthening entire bones.

A British surgeon, Sir John Charnley, introduced the use of plastic implants in orthopedics. He found that high-density polyethylene worked well with metal, and that these materials can be fixed to bone with a cement-like substance called methyl methacrylate. The same compound is used to make Plexiglas.

One of the most widely adopted artificial hip systems was developed by Dr. William H. Harris, Chief of the Hip and Implant Surgery Unit in the MGH

Photographs: Page 1, courtesy of Dr. William Harris; p. 3, (upper left) Scott Davis, (upper right) Clayton Hubbard, (lower) courtesy of Applied Biomedical Corporation; pp. 4 (upper), 8, MGH Photo Lab; p. 4 (lower), courtesy of Dr. Perry Blackshear; p. 5 (lower), courtesy of Dr. Walter Guralnick; pp. 6, 7, Myron Daniels.

Drawing: Page 5 (upper), courtesy of Massachusetts Eye and Ear Infirmary.



Doctor identifies area of burned patient's upper arm covered with artificial skin at left while forearm is covered with the patient's own skin transplanted from another part of the body. Photo at right shows a patch of artificial skin ready for use.

Orthopaedic Service.

Dr. Hugh P. Chandler of the Orthopaedic Service described hip joint replacement as probably the most universally successful implant procedure in his specialty.

"The relief of pain is dramatic," he said. "People whose arthritic hips limited their walking to half a block find after surgery that they can walk a mile or two."

The artificial hip joint consists of a metal ball-and-stem, which replaces the worn top of the thigh bone, and a plastic socket set into the pelvis to receive the ball. Muscles which cross the joint contract to hold the ball and socket in place.

Surgeons use the same metal and plastic to fashion artificial knee joints, but Dr. Chandler said their development lags behind the artificial hip by several years.

Orthopedists often opt to fuse a badly deteriorated ankle joint because joints in the foot help to compensate for lost ankle movement. Many such patients appear to walk normally.

Because the elbow is not a weight-bearing joint, it lags behind both the hip and the knee in development of an assist device.

Some years ago, however, researchers from the MGH, M.I.T., Harvard Medical School, and the Liberty Mutual Insurance Company conceived a revolutionary prosthesis called the Boston Arm to benefit above-the-elbow amputees (*MGH News,* October 1968).

Still in use, manufactured by the Liberty Mutual Research Center in Hopkinton, Mass., but now called the Boston Elbow, the device has undergone many refinements.

The user controls the prosthesis by flexing his biceps and triceps, the degree determined by the speed the brain feels the arm requires. The muscles in turn generate electrical signals to the elbow and its attached artificial arm and hand, telling them in effect what to do.

Surgeons find considerable use for valves of metal and plastic to replace defective or worn natural valves which cause an entirely different sort of muscle, the heart, to fail.

Dr. Mortimer J. Buckley, Chief, MGH Cardiac Surgical Unit, said that until three years ago the medical world thought that a valve taken from a pig would last a minimum of 10 years. "We were disappointed to find," he said, "that deterioration of these biological valves may occur in special circumstances in two or three years, although usually it occurs much later."

Dr. Buckley said a hardware prosthesis may be preferred if the patient can be given lifelong anticoagulation treatment and can be closely monitored.

Dr. W. Gerald Austen, MGH Chief of General Surgical Services, and Dr. Buckley have worked the last few years with a group of scientists led by David M. Lederman, Ph.D., to develop an aortic valve replacement which would not require use of anticlotting drugs.

Dr. Lederman, president of Applied Biomedical Corporation (ABIOMED) in Danvers, Mass., said that in an independent appraisal the Georgia Institute of Technology recently gave high marks to the new plastic valve.

Researchers at the MGH and ABIOMED are also concentrating on development of a totally implantable, electrically driven pump to replace the heart's workhorse, the left ventricle, when it fails (*MGH News,* May 1980).

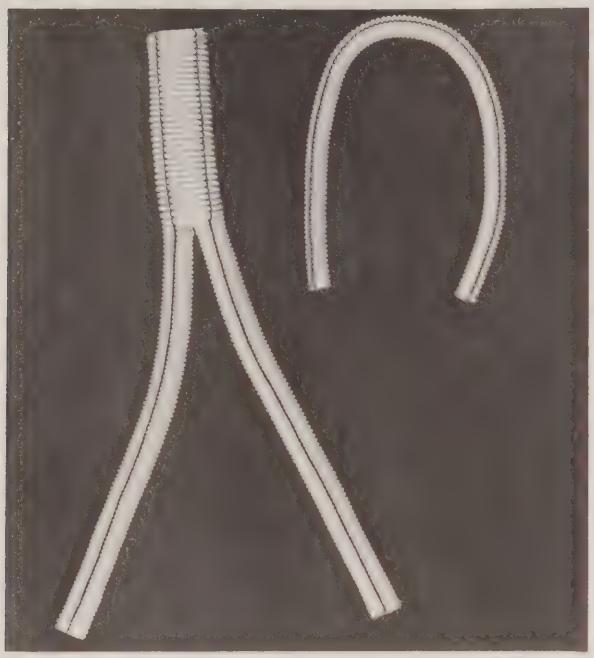
The scientists first successfully tested air-driven models of the heart assist device, keeping calves alive for extended periods of time. "With the collaboration of the Draper Laboratory," Dr. Lederman said, "we are now working to miniaturize all of the system's electronic components so as to make the entire system implantable."

One of the most reliable heart assist devices, one which has already stood the test of time, is the pacemaker

(Continued on Page 4)

Tri-leaflet plastic valve which has undergone extensive testing as a potential substitute for the heart's aortic valve

Synthetic Blood Vessels Prove Invaluable



Made of Dacron, these products can replace damaged portions of the body's larger blood vessels.

(Continued from Page 3)

(*MGH News,* May 1979).

Made possible by invention of the transistor, the pacemaker, implanted in the chest, oversees heart rhythm, cutting in to regulate the beat if it slows excessively.

Around the world, the health of more than 200,000 people of all ages is protected by these small electronic units.

Just as the function of the heart may rely increasingly on assist devices, blood coursing through the heart's chambers may not always be the real thing.

Some medical centers in the United States are trying out a substance called Fluosol-DA in patients for whom a regular blood transfusion is not acceptable. Because of religious beliefs, for example, a Jehovah's Witness will not permit a blood exchange.

Fluosol-DA, which comes from Osaka, Japan, is infused into the bloodstream and, like blood, extracts oxygen from the lungs, then delivers it to tissues throughout the body.

Often referred to as artificial blood, Fluosol-DA contains fluorine and carbon. Since it can be administered without regard to a patient's blood type, the product offers a particular advantage in Japan where only one-half of one percent of the population is RH negative. Finding a natural blood replacement for such individuals would be difficult. In the United States, 15 percent of the population has the RH negative blood type.

Blood vessels sometimes need repairing, and the material used for a graft may be synthetic.

"We always prefer to use biologic materials, such as a section of artery or vein," said Dr. David C. Brewster, an MGH vascular surgeon, "but when you're doing reconstructive work on the large arteries, such as the aorta, it is difficult to find, elsewhere in the patient's body, tissue of sufficient size that can be spared for grafting."

As an alternative, surgeons install man-made vessels most commonly constructed of the porous fabric, Dacron. When tissue heals around the new vessel, cells grow through the fabric and establish a lining of natural tissue inside the channel. Such a lining helps to minimize chances of blood clotting.

Many thousands of women in the United States have undergone surgery for breast replacement following a mastectomy or for breast enlargement. Silicone gel sealed in plastic sacs is placed, not in the breast tissue, but either directly behind it atop the pectoral muscle or under that muscle to sit on the rib cage itself.

Implantable drug infusion pump codeveloped by Dr. Perry Blackshear, now of MGH Diabetes Unit

Dr. Michael Lewis, an MGH plastic surgeon, said the implants have proven to be very safe. However, the body reacts to the implant by forming a layer of scar tissue around the sac, and the natural tendency of such tissue is to shrink. In time, this may give the implant and consequently the breast a somewhat abnormal appearance.

Dr. Lewis cautioned that the implant should not be confused with silicone injections into the breast. Such injections, he said, can cause a severe inflammatory reaction and possible lung problems.

In block form and appropriately shaped, silicone can effectively correct an abnormally developed chin, cheek, or nose. There is even a silicone frame that can be used to make new ears.

Urologists employ a silicone-filled sac, similar to a breast implant, to replace a testicle which may have been removed because of cancer. The problem the surgery solves is strictly psychological.

Many conditions can prevent men from reaching sexual fulfillment. Men who have developed vascular disease, diabetes, spinal cord injuries, multiple sclerosis, and other afflictions may find themselves unable to achieve an erection.

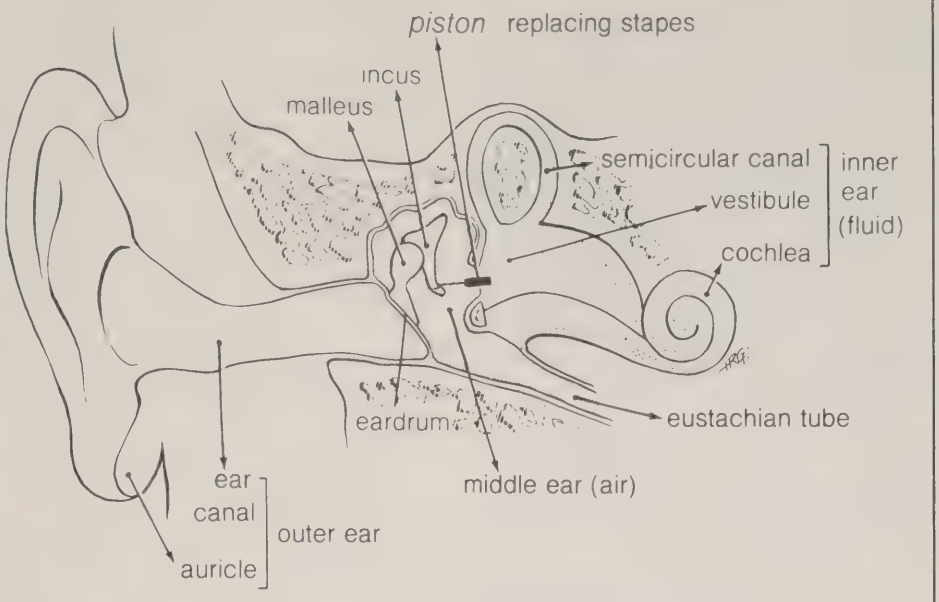
Dr. Niall M. Heney of the MGH Urology Service said penile implants can provide an effective remedy.

One highly successful procedure, introduced about eight years ago, involves surgical insertion of inflatable Silastic tubes under the skin on two sides of the penis. The tubes connect to a tiny pump concealed in the scrotum, and the pump is linked with a reservoir in the abdomen. The patient learns how to manipulate the pump so that a saline solution will transfer from the reservoir to the tubes, making them rigid, and later return.

Dr. Heney said that on occasion the hydraulic fluid may leak, but repairs can be made easily.

For certain diabetics who dread taking insulin daily, a pump smaller than a hockey puck is being tested to take over the drug delivery chore for two weeks at a time.

Invented by Dr. Perry J. Blackshear,



Drawing shows installation of artificial stapes implant which can often restore full hearing to patients with otosclerosis. Stapes is the body's smallest bone.

now of the MGH Diabetes Unit, and a University of Minnesota team headed by Dr. Henry Buchwald, the pump, containing a small drug reservoir, is implanted under the skin of the chest, like a pacemaker. In the trials, involving about a dozen patients, blood sugar levels have been maintained at near normal.

All of the patients developed diabetes during adulthood. Their bodies still manufacture some insulin.

Dr. Blackshear hopes to expand the studies to include 25 diabetics, on pumps or receiving traditional insulin injections at different times.

"We could then determine which method controls blood glucose best," he said, "and whether certain underlying derangements characteristic of diabetes are affected by the new procedure."

Many people with a genetic disease called otosclerosis which causes hearing loss have regained full hearing with the aid of an artificial implant.

Otosclerosis affects the stapes, the third bone in the bone chain behind the ear drum. Moving up and down like a piston, the normal stapes transmits sound from the drum to the inner ear, but in the patient with otosclerosis the stapes becomes fixed.

Dr. Joseph Nadol, an otolaryngologist at the Massachusetts Eye and Ear Infirmary, said a stainless steel-Teflon device which resembles and acts like a piston is installed to replace the natural stapes, and a stainless steel wire atop the piston is extended to the incus, the second bone in the chain. Sound activates the implant.

Work of a more experimental nature is being conducted in the ear to restore lost hearing caused by failure of the cochlea. This is a snail-like organ containing hair cells. They normally transform sound energy into electrical energy which then stimulates the auditory nerve.

A substitute arrangement calls for the patient to wear a sort of headphone behind the affected ear. The phone encodes speech and relays the signals through a transducer which may be situated under the skin. A wire running from the transducer into the cochlea in the inner ear provides the auditory nerve with the stimulation needed to receive the message.

Dr. Nadol said that although work remains to be done on the cochlear implant he thinks it will prove to be valuable for the otherwise totally deaf.

Operations for a cataract — the clouding of a lens in the eye — date back centuries. But after a surgeon "popped out" the lens through a simple incision, the patient always wore thick eyeglasses to correct his sight. Today, after removal of the cataract, the surgeon can implant a plastic lens in the eye, restoring quite good vision without the need for any glasses.

In dentistry, the concept of permanent artificial tooth implants has attracted much interest, but Dr. R. Bruce Donoff, Acting Chief of Oral and Maxillofacial Surgery at the MGH, describes the field as still in its infancy. "There are some things that just haven't received enough clinical trials," he said.

Dr. Donoff, however, praised "mandibular staple dentures," devices designed to help people who cannot wear full lower dentures because of bone deterioration.

Through an incision under the lower jaw (mandible), the oral surgeon inserts a plate which anchors to the bone. Two posts on the plate extend through the bone into the mouth. A bridge can attach permanently to these posts.

False teeth are also getting a new and better look. Dr. Donoff said a new type of ceramic has been produced which may one day replace porcelain in most dental laboratories. The ceramic not only has much better aesthetic qualities, he said, it also has much

(Concluded on Page 6)

A metallic device can be implanted in the lower jaw to anchor lower dentures if the bone has begun to deteriorate.

Dr. Guralnick Assumes New Key Position

Dr. Walter Guralnick, Executive Director of the Ambulatory Care Center, with Melody Hess, Building Coordinator

After 15 years as Chief of the MGH's Department of Oral and Maxillofacial Surgery during which he saw the service rise to national stature, Dr. Walter C. Guralnick reached a decision:

"With so many of my goals having been achieved, I felt that it was time to resign as Chief. Change of leadership at some interval is appropriate and invigorating."

Dr. Guralnick, who has been at the MGH for 30 years, stepped aside but not down.

Although he phased out his private practice, resigned leadership of the MGH unit, and gave up chairmanship of the Department of Oral and Maxillofacial Surgery at the Harvard School of Dental Medicine, he retained his full teaching professorship at Harvard, and he also accepted a brand new challenge.

Since January 1, Dr. Guralnick has served as Executive Director of the still unfinished MGH Ambulatory Care Center. In the near future when fully operational, the nine-level A.C.C. is expected to provide for some 600,000 outpatient visits annually. This figure is more than the combined total of visits at the many doctors' offices and at the nearly half-century-old clinics which the new center is gradually replacing.

"People have always appreciated the advantages of a one-stop health facility," Dr. Guralnick said. "Our new center pulls together many services, offering high quality, comprehensive health care to the community in the most convenient, most comfortable, most innovative manner possible."

Dr. Guralnick was pondering the next step in his career when the A.C.C. Executive Committee asked if he would like to apply for the center's top administrative post. Having been involved extensively with other areas of health care delivery besides his own specialty, he was indeed interested and soon won the appointment.

Dr. Guralnick's background includes a close association with Blue Cross and Blue Shield. In 1950, he was instrumental in establishing the first significant Blue Shield coverage in the nation for oral surgery. He later served six years as a director of Blue Cross in Massachusetts.

He cofounded the Dental Service Corporation of Massachusetts, which insures dental patients, and was its president from 1970 to 1980.

Other organizations which elected him as their president include the Massachusetts Dental Society, Greater Boston Dental Society, Harvard Odontological Society, American Academy of Dental Science, and the New England Society of Oral Surgeons.

In addition to heading a department at the MGH, Dr. Guralnick has served since 1968 as a member of the hospital's General Executive Committee (G.E.C.), Committee on Research, and Committee on Teaching and Education.

From 1974 to 1976, he was Chairman of the G.E.C., the institution's highest ranking medical board.

He also held many important committee assignments at Harvard, including that of Vice-Chairman of the Medical School Faculty Council. The dean customarily sits as Chairman.

Some 20 years ago, Dr. Guralnick conducted the first studies on the immunology of tooth transplants in collaboration with a Harvard Dental School student, Leonard Shulman.

Today, Dr. Shulman codirects the Transplant and Implant Research Unit at the dental school.

The concept of transplanting human teeth is an ancient one, but until Drs. Guralnick and Shulman initiated their research, no one had ever tried to determine whether teeth would act like other human tissue.

"We found they had the same immunological properties," Dr. Guralnick said. "Some patients who received tooth transplants about 20 years ago still have them as functioning teeth."

Dr. Guralnick derives his greatest satisfaction from the success of a five-year Harvard–MGH training program which he instituted a decade ago. The program enables Harvard dental graduates not only to become oral surgeons but also to earn a medical degree and receive general surgical training.

The plan is receiving ever increasing recognition as an important advance in the training of health professionals.

After receiving his DMD degree, the

Artificial Parts

(Concluded from Page 5)

greater strength.

The list of artificial spare parts for the human body continually expands, and a senior surgeon at the MGH predicts the list will grow ever larger in the years ahead.

"Traditionally, much of surgery has been aimed at taking something from the body that should not be there, but now the tide is turning, and we're putting things in that need to be there," said Dr. Paul S. Russell, Chief of the MGH Transplantation Unit and John Homans Professor of Surgery at Harvard Medical School.

Dr. Russell sees no conflict between replacement of failing tissue with healthy tissue, external devices that support life, and synthetic implants.

"Each system has an important role in medicine," he said. "Rather than being in competition, one often complements another." ■

Softening the Impact of New Life-Styles

(Continued from Page 1)

Boston and enlists the help of member-volunteers. Selected to match the patient in age, sex, marital status, and type of operation, the volunteers meet with the hospitalized individual, explain what they themselves went through, and relate how they handled their own difficulties.

Parents of young MGH patients who suffer prolonged breathing lapses in their sleep and are guarded by a heart monitor also find comfort in contacts with other parents (*MGH News,* January–February 1979). An association formed by them to enable them to share their feelings has regional chapters in several states.

Another group of parents, those whose children are to undergo open heart surgery, meets at the hospital to get professional information and to help one another.

Dr. Silverman conducted a pilot study among a small number of people, members of self-help groups, who either had undergone removal of their voice box (laryngectomy), or were receiving blood-cleansing kidney dialysis, or had babies afflicted with a crippling spinal defect (spina bifida). In the long run, all had accepted offers of visits from volunteer helpers, but initially a few had said "no" to the proposals.

Dr. Phyllis Silverman (far right) addresses gathering of health care professionals and members of self-help groups at MGH-sponsored workshop.

The initial negative reaction came from people unable to admit the seriousness of the problem they were facing. When they finally began to comprehend the adjustments that lay ahead, they realized they had to find out more and were glad then to talk to the visitor.

Author of the books, "Helping Women Cope With Grief" and "Mutual Help Groups: Organization and Development," Dr. Silverman also was closely associated with a Widow-to-Widow program initiated by the Laboratory for Community Psychiatry at Harvard Medical School and edited a book, "Helping Each Other in Widowhood."

As a researcher for the Harvard laboratory, Dr. Silverman was asked in 1966 to determine what services were available to widows. She found that except for professional counseling sought because of psychological distress, there were really no services that addressed

(Concluded on Page 8)

individual accepted into the combined program serves as an oral surgical resident at the MGH during his first post-graduate year. He attends Harvard Medical School the second year. Then he devotes six months to general surgical training at the hospital followed by six months in oral surgery. The fourth year finds him serving as a second year resident in general surgery and, finally, in his last year of training he becomes chief resident in oral surgery.

The concept of combining a medical degree and general surgical training for oral surgeons was pioneered by Dr. Guralnick and Dean Paul Goldhaber of the Harvard School of Dental Medicine.

Not only is the MGH program successful, it is also unique. Its participants receive more general surgical training than is available under any other plan, Dr. Guralnick said, and the students spend only one year out of the five in medical school to complete their MD requirements. This is possible because Harvard dental and medical students take their preclinical studies together.

One of the earliest graduates of the combined degree program, Dr. R. Bruce Donoff, became Acting Chief of the Departments of Oral and Maxillofacial Surgery at both the MGH and Harvard Dental School when Dr. Guralnick relinquished the two positions.

In recommending Dr. Donoff, who had been his second-in-command for a number of years, Dr. Guralnick described him as outstanding in patient care, teaching, and research. Dr. Donoff had developed a national reputation and had a choice of attractive professional opportunities.

In his new MGH capacity, he directs five full-time and at least a half dozen part-time staff oral surgeons. Six residents also rotate through the service.

Together, the doctors care for between 500 and 600 inpatients and about 7,000 ambulatory care patients annually.

Under Dr. Guralnick's guidance, the department has attained such acclaim that today at least 50 applicants are considered for each resident vacancy.

Many of the department's graduates also have moved into key posts elsewhere. They include department heads at Columbia–Presbyterian Hospital in New York, Brigham and Women's Hospital and Children's Hospital in Boston, the Kaiser Foundation and Martin Luther King Hospitals in Los Angeles, and Mary Hitchcock Hospital, affiliated with Dartmouth Medical School, in Hanover, N.H.

Other graduates have received important faculty appointments at such schools as the Universities of Chicago, Oregon, and Connecticut.

Wherever they went, Dr. Guralnick's students carried with them a close attachment to their former mentor. In offering the benefits of his expertise, he also exudes an unusual amount of personal warmth. Always accessible and interested in what one has to say, he has made close friends throughout the MGH.

In launching Dr. Guralnick on his new career as operator of the Ambulatory Care Center, the MGH Trustees gave him a mandate:

"Make it self-sufficient." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Widow's Program Typifies Helper Concept

(Concluded from Page 7)

themselves to the personal problems of widows.

"As I spoke to more and more women who had lost their husbands," she said, "I realized that most were telling me, 'Really, the only one a widow can talk to is another widow.' "

Friends and relatives would tell the bereaved person, "You'll be okay . . . Everything will work out." The assurance had no real meaning; yet, everyone was impatient for the grief to end.

Dr. Silverman said that just as a person with a spinal cord injury, who was once strong, outgoing, and athletic, must get used to never walking again, so, too, must a widow develop a new sense of herself in order to live again. This does not happen overnight.

Five widows recruited by the Harvard laboratory reached out into a community to offer help to other widows and received a 60 percent acceptance response. "The figure was quite impressive," Dr. Silverman commented, "since no precedent existed for such a program."

The women who were contacted needed to know mostly that they were not alone, that others their age had experienced the same sadness and trials.

One widow with three children under 6 was constantly occupied with their needs. A simple suggestion by another widow to hire a neighborhood teenager to baby-sit one afternoon a week enabled the mother to get out for a change.

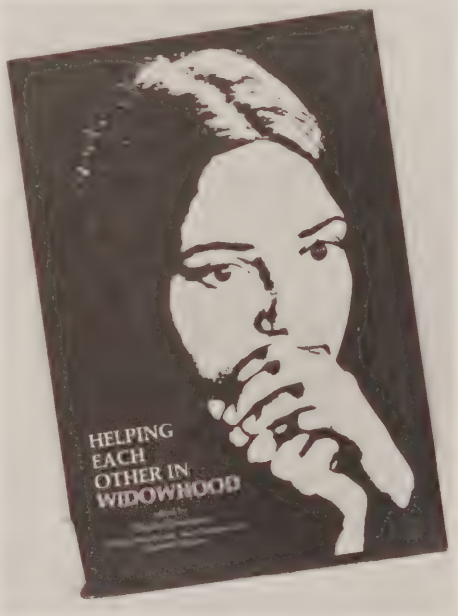
The mother also could not understand why her children were beginning to act resentful toward her. The widow who befriended the mother explained that by trying to be strong and shedding no tears the mother was giving her children an impression she did not miss their father. She was assured that crying together was healthy.

The eldest boy in the family needed some support as well. Somebody at the father's funeral had told the child, "You'll have to take daddy's place now. You'll have to be the man in the family." The 6-year-old became distraught at the idea of such responsibility. He felt much relieved on being told he did not have to assume the family burdens.

One widow who attended a group meeting with other widows admitted to everyone's surprise that she was glad her husband died. He had kept the household in a very tense state, laying down and enforcing very strict rules of behavior. "We lived a very empty, barren life," the woman said, "but now my children and I are more relaxed. We frequently have guests in our home. And I feel guilty."

The widows with whom she met gave her what she needed, permission. "You have every right to build a life that will be good for you and your family," they assured her. "You don't have to feel guilty."

The program launched by Harvard's Laboratory for Community Psychiatry has mushroomed. Groups promoting the principle of coming together and helping one another have become established nationwide.



Widow-to-widow aid programs extend nationwide.

The American Association of Retired Persons developed a widowed persons' service, designed to aid both wives and husbands who lose spouses. The association sends consultants into communities to help organize assistance groups.

Dr. Silverman mentioned a hospital in New Jersey which sponsors a self-help clearing house within the institution. The clearing house receives more than 2,000 telephone calls a month from individuals seeking contact with a self-help organization of one kind or another. The center furnishes information on more than 200 such groups.

While considerable data have been compiled attesting to the productiveness of these outreach programs, little information has been gathered about the person who rejects offers of assistance.

Dr. Silverman, who is also a Lecturer on Social Welfare at Harvard Medical School, hopes to conduct research in this gray area at the MGH Institute of Health Professions.

"There are many ways of being helped," she said. "Very often widows who turned down help either already knew other widows from whom they could solicit advice if necessary, or they were well-read people who felt quite capable of solving their problems themselves."

But the issue goes deeper, Dr. Silverman said. In the long run, for example, does the person trying to make a self-adjustment unaided achieve as good a quality of life as the individual who has accepted support and guidance?

And what motivates people later to affiliate with self-help groups?

In her writing, Dr. Silverman prefers the term "mutual-help" to "self-help." "After all," she explained, "there really is a mutuality in the self-help concept.

"When people see that the support they get comes from others just like themselves, something often induces those who are helped to one day become the helpers." ■

MGH News

Vol. 41 No. 5 MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS June–August, 1982

Preserving Special Attributes in a Changing Time

Demands Upon a Pianist Take Their Toll

Concert pianists are usually not considered super athletes, but in a sense that is exactly what they are.

Music lessons begin early, but pianists generally do not gain national recognition until their early twenties. And once they have established a reputation, their careers often span another 50 years.

Throughout this time, virtuosos and aspiring virtuosos practice six to eight hours a day, seven days a week. A popular artist may perform 100 concerts a year and also make recordings.

By comparison, the lifespan of professional athletes is brief. They reach the peak of their ability by their early twenties and are in the limelight typically for four or five years. Only the super athlete remains at the top of his prowess for 10 years or longer. What's more, the playing season is shorter than that of a concert soloist.

Given the tremendous physical demands on professional pianists, it is no wonder that many develop problems with their hands — problems that eventually may cripple their concert careers. Pianists take it as a matter of course. They adapt until it becomes impossible.

Until recently, understanding of the musician's hand and of its difficulties was limited to works culminating in the monograph of Otto Ortmann, *The Physiological Mechanics of Piano Technique,* published almost 50 years ago.

For the past two years, a team of MGH physicians – Drs. Fred H. Hochberg, Robert D. Leffert, and Bhagwan T. Shahani — has labored to understand these difficulties and to provide treatment for them. These physicians are often found next to the piano in the MGH chapel.

They have treated more than 50 musicians for occupationally related complaints and corresponded with another 80. "The complaints of our patients are somewhat sophisticated," said Dr. Leffert, an orthopedic surgeon and Chief of Rehabilitation Medicine at the MGH, "because the functional needs of these patients are highly specialized."

The physicians, listening to descriptions of symptoms, found that translating the complaints into medical terms was especially difficult. "Most often we are asked to obtain musical histories to define medical complaints," explained Dr. Hochberg, a neurologist.

Although some musicians complain

(Continued on Page 5)

Rigorous practicing at the keyboard can over time cause serious hand problems.

Dr. John Robert Buchanan, the incoming MGH General Director, appears to arrive at an institution's hour of need.

Sometimes the need is an unusual one — like the lack of a crew in college. What does a 6-foot, 7-inch collegian do when he wants to participate in a sport that Amherst College dropped in the 70s — the 1870s?

If his name is Buchanan, he and a classmate revive the tradition. They did and wore the Amherst colors in the late 1940s.

At Cornell University Medical College he was dean during the student activism which gripped the nation's colleges in the early 1970s.

And at Michael Reese Hospital, Dr. Buchanan arrived in 1977 when the hospital's finances were suffering. They have turned around during his leadership.

His appointment at the MGH comes one-third of the way through a $114 million fund-raising campaign and at a time when high costs and government regulations are threatening teaching hospitals. Dr. Buchanan brings no preconceived specifics to confront forces buffeting the MGH.

"The MGH is one of a very small group of premier medical institutions," he said. "My principal responsibility will be to maintain the special qualities that have put this hospital in its position."

The changing tenor of the times, however, will constrain any chief executive officer.

"In the past," Dr. Buchanan said, "the resources were there to do almost anything the institution wanted, and a high percentage of attempts succeeded.

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Susan A. Gertman, *Reporter*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
Joseph B. Martin, MD, *Interim General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIALS:

A Salute to Dr. Martin

Dr. Joseph B. Martin has carried out in outstanding fashion his duties as MGH Interim General Director. He has advanced the hospital on several difficult fronts and achieved this diplomatically. When Dr. J. Robert Buchanan (page 1) relieves Dr. Martin of those duties July 1, the interim leader will return full time as Chief of Neurology and to his brilliant research career. We salute him.

For Concert Artists: a Glimmer of Hope

Of mankind's many achievements none distinguish homo sapiens more than the culture he has created. Art, music, literature, and the like set us apart from "lower beings." Whether we gaze at a sculpture by Michelangelo, listen to a Beethoven string quartet, or watch a play by Shakespeare; whether we stroll beside the Parthenon or read a novel by Dostoevski, the experience can prove electric. Products of man's culture inspire and stimulate, and provoke joy and sadness. They entertain. And they make us earthlings think.

In most fields the artist communicates directly through his creation. The author writes, and a printing press multiplies the fruits. Or an artist paints a canvas or wall. We can view directly the painting or sculpture, or we can transport ourselves mentally by looking at a copy. In fields like art, architecture, and sculpture, reproductions lack the authenticity of the original. Surely a flat copy of a van Gogh can never convey the feeling of the impasto in the actual painting.

In music there are essentially two acts of creation. The first comes when the composer jots black notes on composition paper. The second follows with the performance by the musicians with or without the conductor's intervention. Nowhere in classical music is this duality more manifest than when the soloist improvises in a cadenza. The very training needed to become a top soloist itself consumes so many thousands of hours. When after so much dedication, a disability prematurely ends a performer's career, the result is an irreplaceable loss for the classical music public and a tragedy for the artist.

To reclaim even one soloist to the concert stage would be an unexpected gift to both public and artist. That is why the pioneering work of three MGH specialists provides them with such satisfaction. A page 1 article in this issue describes this labor of love. For those expecting sudden, dramatic results from their treatment of musicians, there are no miracles. Only plodding improvements. But with each new patient the physicians add a wrinkle here, a nuance there. Already their findings and innovations are providing a glimmer of hope for future generations of concert greats — hope for both prevention and treatment — hope that did not before exist.

New MGH Director Calls for Guidelines On Intensive Care

(Continued from Page 1)

With dwindling resources available, we now have to be more discriminating from the start. We must make judgments about high payoffs in expensive technology instead of choosing technology that won't do that much to improve patient care. Such an approach, however, does not apply to basic research because by its nature fundamental research defies attempts to predict its outcome. Having basic research next to patient care stimulates questions and answers that benefit both."

At the same time, Dr. Buchanan clearly sees that the primary role of a teaching hospital is to provide excellent care for patients. Research and teaching follow.

The incoming leader worries that the public has some false ideas about the cost of that patient care.

"Can the MGH deliver at a lot less money the quality of care it now offers?" he asks. "I doubt it. Actually the cost issue has another side. The public really has some serious questions to ponder. Should, for example, people whose devastating illness can't be changed all that greatly be given intensive care?"

When he arrived in Chicago five years ago, the fiscal problems he faced there were serious and immediate. He brought with him a strong grasp of the elements of health care finance.

"What he didn't already know, he was quick to pick up and remember," said John Gunn, Michael Reese's chief fiscal officer.

Harold H. Hines, Jr., was the Chairman of the Board of Trustees in those difficult early years:

"Bob restored the fiscal confidence so necessary to the supporters of Michael Reese and the Board and the staff. He did a remarkable administrative job to put us on our present favorable fiscal track."

The result was an impressive "A1" rating when Reese next went to the bond market.

The fiscal acumen that has made the

Photographs: Page 1, MGH Photo Lab; pp. 3, 4, courtesy of Dr. J. Robert Buchanan; p. 5, Alan Lucas; p. 7 (upper), 8, Myron Daniels.

Chicago hospital healthy impressed the state legislature of Illinois. A series of health care bills brought Dr. Buchanan repeatedly to the legislature last spring and summer. Mr. Gunn credits Dr. Buchanan with persuading the legislature to alter bills that would have crippled provision of outpatient care by Illinois teaching hospitals.

"Within Michael Reese, he was always tough in containing the budget," Mr. Gunn said. "He persuaded people that fiscally viable budgets are essential. As a result our budgets went up only seven percent last year during double digit inflation."

Dr. Buchanan managed such difficult matters with what Mr. Hines, the former Board Chairman, called gracious firmness.

"He has the capacity to lead and command," Mr. Hines said, "without being offensive and autocratic. He's a truly remarkable man. He can make tough decisions, say 'no,' pay the price, and then move on.

"The medical staff has the highest regard for his integrity, judgment, and ability to look at the future. He's an effective long-term planner."

One member of the medical staff, Dr. Martin Swerdlow, Chairman of Pathology, worked with Dr. Buchanan on several internal and external committees.

"He understands and cuts through the flak in a direct way and recommends what seems like an appropriate approach," Dr. Swerdlow said. "Often it is not so much a decision but a process for arriving at a decision. He's always sensitive and puts himself in the position of whoever faces the dilemma."

The high esteem in which the medical staff holds him appears to pervade the institution. Concern for individuals and a retentive memory play a role.

On one occasion Dr. Buchanan learned that a woman employee was saving the hospital money through astute purchasing practices. He tucked the information away until he met her for the first time six months later.

"Oh, you're the young woman who's saving us so much money," he said, "and we appreciate that."

Dr. Buchanan has an easy manner with employees. He customarily talks with the receptionist at the information desk, the nurse on the floor, the man who changes the light bulb, and the service chief.

In his early days at Michael Reese, he wandered from floor to floor to meet employees. On one such trip he observed a young nurse who was particularly good with patients.

Dr. Buchanan with patient at New York Hospital's Outpatient Department (early 1960s)

In chatting with her, he learned she was frustrated in her quest to earn a graduate degree because of her conflicting hospital shift. When Dr. Buchanan returned to his office, he suggested that nursing change her shift.

Always trying to improve morale, he recently cleared the way to renovate the Michael Reese employees' cafeteria. For patients and employees alike he stresses the need for a good physical and psychological environment.

Dr. Buchanan worries that some groups can easily feel isolated in a hospital environment.

"Groups that do not provide direct patient care," he said, "are nonetheless terribly important to the function of a hospital. They're the concrete foundation on which an institution rests. They need feedback, an accurate assessment of what they do so that they can understand their importance."

Bicycling with son, Ross, in 1971

Dr. Buchanan's typical work day begins around 7 a.m. when he arrives from his modern north side Chicago home. His office also reflects modern taste from the beige rug to a brown Picasso print.

Seated in an upholstered chair at a combination desk-table, he writes, and he dictates answers to yesterday's mail. When a secretary comes in at 7:30, he goes over with her his appointments schedule and his travel arrangements. Around 8 the other administrators usually consult informally with him. By 8:30 or 9 he plunges into appointments and meetings.

Various members of his executive staff regroup in his office between 5 and 6 p.m. After cleaning his desk, he leaves around 7 p.m. After dinner at home he attacks the briefcase of reading he brings from the office.

That sort of day leaves little time for hobbies. He has few: occasional horseback or bicycle riding. Infrequently, he dabbles in photography. An excellent chef, he is frustrated by lack of time.

"I'm too impatient to watch organized sports," he admits.

His family enjoys pets. Daughter Allyn Hamilton Buchanan, 13, owns a cockatoo and a skunk. Son Ross

(Concluded on Page 4)

Christmas 1981. With wife, Dr. Susan Buchanan; son, Ross; and daughter, Allyn. Dr. Buchanan will become General Director on July 1.

On Dr. Buchanan:

"He Has Extremely Good Insight Into People"

(Concluded from Page 3)

Townsend Buchanan, 16, has a green-wing macaw, and Dr. Buchanan himself has a blue-headed Amazon parrot that calls him Bob.

His wife, the former Dr. Susan Townsend Carver, who works at the American Medical Association in the Group on Medical Education and Scientific Affairs, shares responsibility for the pets belonging to the entire family: a French poodle and several horses that graze on their Connecticut farm.

The incoming General Director enjoys reading historical novels and biographies and delights in the foibles of the academic world of C. P. Snow.

He does not smoke and drinks only socially. While he confesses to two addictions, he indulges in one sporadically and shuns the other.

He refuses to read mystery novels because he "can't put them down." While he enjoys eating, he diets chronically. Chocolate is especially difficult to resist. With the aid of long, fast legs with which he tears about the hospital, he helps to keep his weight between 205 and 210 pounds.

He brings to his outside organizations the same fascination with work that drives him at Michael Reese. His biographies in *Who's Who in America* and *Who's Who in the World* list only a portion of the many voluntary institutions and boards on which he serves part time.

Said Dr. Patrick Ongley, the President of one, the China Medical Board:

"He serves with dedication on a number of our committees. He shares with us a wide knowledge of education and has extremely good insight into people. He's especially helpful in long-range planning.

"We've traveled together in the Far East three times. He's always bright and cheerful even under very difficult circumstances. He has an ability to get along with people from whatever country. And he has a sympathetic approach to their needs.

"When we all write reports at the end of a trip, I know Bob's will always be thorough and thoughtful."

Dr. Buchanan has had more experience in China than most Americans. Has he learned Chinese? Laughed Dr. Ongley:

"He was a dead loss in ordering a decent American breakfast in China." ■

Tour of Army Duty Altered His Career

Dr. Buchanan's father was president of a major national corporation.

Goal-oriented and successful, he endowed his son with a need to use his talents for the public good. From his mother he derived a quiet strength and perhaps something more. Despite her strong will, Mrs. Buchanan had a severe chronic disease. Her illness may have subtly influenced her son's career in medicine.

If so, Dr. Buchanan himself is unsure. His early performance in school was good but not exceptional. At Amherst his grades kept improving enough to earn a cum laude graduation. There the honors program in biology stimulated an interest in research. The experience transformed a proclivity toward architecture into a thrust for medicine.

After graduation from Cornell University Medical College, he trained as a resident and research fellow at New York Hospital and became an endocrinologist.

For a time Dr. Buchanan considered a career in research but recognized he lacked patience.

Dr. Buchanan first tasted health care administration during a mandatory

It was during an Army tour of duty that Dr. Buchanan (right) became interested in hospital administration.

Efforts to Understand Pianists' Problems Can Be Difficult

(Continued from Page 1)

of pain, numbness, tingling, or weakness, most couch their difficulty in terms of musical technique. They complain of the now unplayable octave passage in a second movement of Brahms. Or, they might say, "My teacher says that I am having difficulty with arpeggios in my new pieces."

Because of the specialized nature of their problems, musicians are often frustrated in seeking medical attention. Early difficulties are often confused with severe, progressive neurological disorders. Others have been told they have an "occupational neurosis," "battle fatigue," or a psychiatric disorder that expresses itself in an inability to use the hands. Not uncommonly, blame is placed on the complexity of a particular piece.

In fact, based on the MGH experience, these diagnoses are rarely accurate. Pianists treated by the team have rarely had a progressive neurological disease or psychological disorder.

Although the pianists themselves often see their problem as one of technique, Dr. Hochberg said that he has yet to meet a performer who has not at one time mastered the problem that he or she presents. "More often than not the musician will say, 'I used to be able to play this Beethoven, now I can't.' "

Involuntary curling of the fourth and fifth fingers of the right hand is one of the occupational hazards of being a concert pianist.

Gary Graffman, a winner of the prestigious Leventritt award and a leading American pianist, was one musician who was told that he might have "battle fatigue" when he consulted a series of doctors for a hand problem he had lived with for 2½ years. Finally, a friend of his asked Dr. Hochberg if he would see the pianist and try to think through the problem.

When Mr. Graffman came to the MGH, the doctors examined him to rule out the common causes for hand difficulties. Electrodiagnostic studies showed no damage to nerve or muscle function. Once that was done, Mr. Graffman was videotaped playing the piano. "The videotape has helped us immensely," Dr. Leffert said. "It allows us to go back and watch the pianist's stance, hand, and arm movements. It has made it easier for us to begin to separate their problems."

The pianist also taught the doctors a trick that they now use in their examinations. The doctors recall, "One of us said to him, 'What is normal?' and he said, 'I'll show you what normal is; it is in my left hand.' And at that point we began to use mirroring to compare, using the same piece played with the right and left hand, what was happening to the fingers on one hand versus the other. And this led us quickly to begin to spot exactly what the difficulties and compensations were."

Mr. Graffman's problem was diagnosed as one of motor control of the

(Concluded on Page 6)

Army tour of duty. It was somewhere between Seoul and Inchon, Korea, in 1958 and 1959 that he served as Chief of Medicine and Chief of Professional Services for a large military hospital.

"I realized I was not going to be a great researcher," he said. "I thought I was a pretty darn good physician, but I didn't feel this ability was all that rare."

Back at Cornell again, he served as an outpatient administrator and spent several months on a World Health Organization Fellowship. He accepted an opportunity to become Executive Dean at Cornell while both directing the ambulatory program and teaching. In 1969 he became Dean, a post he held until 1977 when he went to Michael Reese.

His achievements as an educator have been significant. At Cornell he was instrumental in charging the committee which revised extensively the undergraduate medical school curriculum and established an M.D.-Ph.D. program with Rockefeller University. While a member and later chairman-elect of the Council of Deans of the Association of American Medical Colleges, he participated in the founding of the Association's Management Advancement Program.

He continued his educational commitment at Michael Reese by simultaneously serving as the Associate Dean of the University of Chicago. Nor has he confined his educational interest to this country. Besides his efforts in China, he has been involved in medical education development in Brazil, Iran, and Jamaica.

Gradually he has ceased seeing patients, and he's become a full-time administrator. But former patients know how to reach him at home.

"I love taking care of patients," Dr. Buchanan said. "But at this point I'm not sure it's fair to them unless I have more time to devote to them and to keep up with the professional literature."

As an administrator Dr. Buchanan has probably made a greater contribution to patient care, research, and teaching than if his career were concentrated on any one of those areas. His effective management has stimulated all three at Michael Reese. At the same time, his considerable success as a fund raiser has nourished the triad.

Despite his clear choice of career he does not really regard himself as a card-carrying hospital administrator.

"I'm a physician who has accumulated experience in a variety of executive functions of a large medical institution. I would have difficulty if an institution weren't large and sufficiently diversified to justify experts in highly technical areas about which I know little." ■

A Troubled Pianist Finds He Is Not Alone

(Concluded from Page 5)

extensor muscles of the right fourth and fifth fingers. The fingers were so weak that they curled involuntarily into the palm, making it difficult for the artist to clear these fingers from the keyboard.

Mr. Graffman believes his problem started many years back when he sprained his fourth finger while playing on a dull piano. To compensate for the injury, he changed his fingering and began to play octaves with the first and third fingers instead of the first and fifth. It worked beautifully for a while, and then, suddenly, it stopped working.

Once the problem was diagnosed, Mr. Graffman was given an exercise brace designed to strengthen the muscles that had begun to waste away after years of tucking under the fourth and fifth fingers. The pianist is now being evaluated by Drs. Shahani and Michael J. Kaminski who hope to retrain his finger control.

Drs. Leffert and Hochberg treated Mr. Graffman and were ready to stop there, thinking that his was an isolated problem. But shortly after the pianist came to the MGH, his memoir, *I Really Should Be Practicing,* was published by Doubleday.

The favorable reviews of the book coincided with announcements of his canceled concerts. Articles about Mr. Graffman appeared in many newspapers and invariably detailed his hand difficulties and treatment at the MGH.

It turned out that Mr. Graffman was not alone in having hand problems. "The article in the New York Times *led to a slew of phone calls from pianists around the country who recognized that they were not unique in having difficulties," Dr. Hochberg said.*

The pianists told the MGH physicians that they had a similar problem and that their doctors couldn't help them. "At this point," the neurologist said, "it became apparent that we were dealing with an epidemic."

Three-quarters of the patients have had tendinitis, an inflammation of the fibrous tissue which connects muscle to bone — in this instance in the hand.

The remaining musicians had arthritis or various syndromes. About five percent have suffered from carpal tunnel syndrome, a condition that occurs when swollen tissue presses against the median nerve which transmits feeling to the hand. The result: pain and numbness.

Two patients have had thoracic outlet syndrome, a problem in which the blood supply to the arm and neck is restricted because of having to hold certain positions while playing. And several have had what Dr. Hochberg called the over-use phenomenon, a problem that resolves itself after a respite from playing.

More than four-fifths of the patients have been pianists, although the physicians have also treated cellists, violinists, harpists, and viola players. The vast majority of pianists have had right-hand symptoms, probably because the right hand normally predominates in the more highly ornamented passages and operates in the weakest area of the instrument.

The musicians have ranged in age from 18 to 70 with the median age in the late thirties. On an average, the musicians have played 23 years before they recognized a problem, and there were nearly as many women as men in the group.

With the exception of two jazz players and one rock-and-roll performer, all of the pianists have been classical artists. The reason, according to the doctors, is that "It is much harder for someone with an impairment to conform to the rigid requirements of the classical piano than to improvise. Not surprisingly, even these three pianists had classical training."

The doctors began to look for the origin of the hand problems in the player's technique and found that most of the patients belonged to the Russian School which emphasizes strong, individual finger movements. Calling themselves "steel-fingered" pianists, they tended to play "large" pieces by such composers as Rachmaninoff, Liszt, and Brahms — compositions that show off their technical brilliance but that also require considerable strength and speed in the right ring and little fingers.

To play octaves, the pianists also tended to use ulnar deviation, a position in which the hand is cocked outward. "Ulnar deviation is the worst position to play in if you want to maintain fourth- and fifth-finger extension," Dr. Hochberg said.

One of the problems of mastering a difficult piece, such as the Brahms D-minor piano concerto, is that the pianist may be inclined by his own expectation to play the music for the next 50 years.

The MGH neurologist, who is also an Assistant Professor of Neurology at Harvard Medical School, said that pianists with severe hand problems can play most of the Bach repertoire because the music is less involved with extended hand positions and octaves.

Before coming to the MGH, some of the musicians had undergone as many as six operations to correct their hand problem. Others had been through a variety of therapies, including cortisone injections in the elbow and wrist, hot wax treatments, physical therapy, piano therapy, L-Dopa (a drug for Parkinson's disease), and DMSO (a controversial treatment for arthritis). Trials of hypnosis and anti-depressants provided only temporary relief.

When a musician comes for treatment, Drs. Hochberg and Leffert search for conditions that might cause problems, such as nerve entrapments, arthritic changes, or tendon difficulties. Nearly all patients undergo electrophysiological studies to determine if there is nerve or muscle damage. Only two patients have required surgery.

The medical team needs more sophisticated means of documenting a performance and hopes to acquire the facilities for computer analysis of movement — a Selspot apparatus.

Because each musician presents a unique problem that is determined by his or her hand structure, length of practice sessions, and repertoire, the medical team has made use of a number of different treatments, including anti-inflammatory medications, splinting or other physical therapy devices, restrengthening exercises, biofeedback, and such modifications in routine as rest and change in position.

Part of the problem might be alleviated if pianists knew about the anatomy of the hand. "Virtually no musical training program includes any consideration of the anatomy of the pianist's instrument, his hand. They know about the piano, but they do not know about their hands, arms, and shoulders and about the requirements for muscular activity and performance," said Dr. Leffert, who is also an Associate Professor of Orthopedics at Harvard Medical School.

Reviewing the progress they have made so far, Dr. Hochberg said, "If nothing else, we have removed some of the myths shrouding hand difficulties. The stigma that used to be attached to a pianist who was unable to play a piece is beginning to disappear." ■

Search for the Cause Of a Strange Disease Centers in Venezuela

Working in 40°F environment, Dr. James Gusella supervises a process which transfers DNA samples to a special paper for later identification of possible genetic markers.

Some 120 years ago a Spanish sailor decided he had had enough of the sea and abandoned ship in the Venezuelan seaport of Maracaibo.

Anton Doria began a new life and a family, but then he died of a peculiar and mysterious illness.

Little could this ex-mariner with simple ways and wants have imagined that, because of his disease, United States and Venezuelan investigators would one day be delving intimately into the lives of his descendants.

Mr. Doria had Huntington's disease, an inherited disorder in which brain cells deteriorate (*MGH News,* November 1979). Victims gradually lose control of their minds and bodies. Death occurs 15 years or so after symptoms initially appear. Children of an afflicted person face a 50-50 risk of developing the malady.

Doctors estimate that in the United States and Canada at least 100,000 people either have the disease or have reason to fear that they will.

What then is so special about Anton Doria and his successors? Unlike most families in which Huntington's disease has been traced back many years, few members of the Doria clan have gone their separate ways.

More than 1,000 Doria descendants reside in a chain of small villages rimming Lake Maracaibo in northwestern Venezuela. The population is one of the largest concentrations of Huntington's disease families in the world.

Through this group, American and Venezuelan researchers hope to identify the disease-causing gene for the first time. Tests might then be possible to detect the malady before serious neurologic changes take place.

In July 1980, the National Institute of Neurological and Communicative Disorders and Stroke signed a contract with Venezuela's University of Zulia for the collaborative investigation.

During two visits to the Lake Maracaibo area, the latest in March of this year, an American team of neurologists, geneticists, anthropologists, and other specialists collected blood and skin samples of well over 500 relatives of the one-time Spanish sailor.

Dr. Richard W. Erbe, Chief of the Genetics Unit in the MGH Children's Service and a member of the study team, carried the specimens back to his unit for analysis by James F.

(Concluded on Page 8)

Why Schumann Gave Up a Concert Career

Robert Schumann (1810–1856), one of the great German virtuosos, was one of the first pianists known to suffer hand difficulties. Although there is some debate concerning the origin of Schumann's injury, Dr. Fred H. Hochberg, an MGH neurologist, believes that the musician had symptoms of a syndrome that afflicts pianists.

In 1831, at the age of 20, Schumann wrote in a letter to his mother, "I have overdone my technical studies resulting in the maiming of my right hand. Some fingers, no doubt because of too much writing and playing in earlier years, have become quite weak, so that I can hardly use them."

Schumann's injury may have been caused by a device he designed, "my cigar box," to immobilize the third finger while exercising the fourth and fifth. Instead of increasing dexterity, the sling may have crippled the third finger by straining the tendons. This injury led the pianist to abandon his concert career and devote himself to composing.

The reason that music literature does not mention hand injuries until the mid-nineteenth century may lie in the history of the piano.

When the modern grand piano, with seven octaves and an iron frame, came into use in the mid-1800s, it required a whole new system of fingering. The earlier harpsichord and clavichord were played with the second, third, and fourth fingers, rarely with the fifth and almost never with the thumb.

Robert Schumann

The new instrument also gave rise to a class of virtuoso performers who vied for increased facility.

Another popular method for increasing dexterity was a surgical procedure called a tenotomy. Developed by Dr. William Forbes, a surgeon, in the mid-nineteenth century, the operation called for a one-quarter inch incision to sever the tendons linking the fourth finger. Tenotomies were popularized by Eugene Bonelli, who traveled across the United States in the 1890s, setting up shop at music gatherings and performing the 15-minute operation on all comers.

The procedure did not succeed in strengthening the fourth finger and eventually lost popularity. It is rarely used today. ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114
Address Correction Requested

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

DNA Variations May Lead to Disease Gene

(Concluded from Page 7)

Gusella, Ph.D., a geneticist, who is a member of the Children's and the Neurology Services.

From the samples, Dr. Gusella is extracting DNA (deoxyribonucleic acid), the chief chemical component of genes which are the basic units of heredity. In most healthy individuals the DNA sequence appears pretty much identical. Dr. Gusella's interest is in finding variations in the sequence.

"I am looking in the same family for variations that are coinherited a high proportion of the time with the Huntington's disease gene," he said.

These variations, or genetic markers, could turn out to be other genes linked to the one responsible for Huntington's.

Dr. Gusella said that although the genetic marker that goes along with Huntington's has not yet been found "we clearly have many DNA sequences that vary from person to person in this Venezuelan population, and when you follow enough of these markers, you eventually will find one that is linked to a given disease."

Dr. Erbe said that the computer printout of the Doria family tree "already is long enough to cover the entire wall of a good-sized room."

Dr. Gusella's work is funded in part by a unique multi-institutional "Center Without Walls," established in Massachusetts in July 1980, to advance understanding and treatment of Huntington's disease.

Drs. Joseph B. Martin, MGH Chief of Neurology, and Robert G. Feldman, Chief of Neurology at University Hospital in Boston, are Director and Associate Director respectively of the Center, made possible by a grant from the National Institutes of Health.

When the study in Venezuela began, 29 individuals were known to be related to Anton Doria. About half bore the illness that took his life. Of the hundreds of other people now listed in the pedigree, the number with the disease remains uncertain because many who do have the gene are still too young to express the affliction.

The condition can appear at an early age, however. When that uncommon event develops, progression of the symptoms usually is rapid and severe.

In Venezuela, Dr. Erbe came upon an 8-year-old boy who appeared to be only two or three years away from death from Huntington's. Although the child's body had not yet become grossly affected, he was already suffering serious neurological impairment.

In its latest trip, the American team journeyed four hours by boat to an unusual village named Laguneta. It consisted of 50 or so houses perched on stilts above the waters of Lake Maracaibo. Dense jungle and constant swarms of insects prevented human habitation on land in that area.

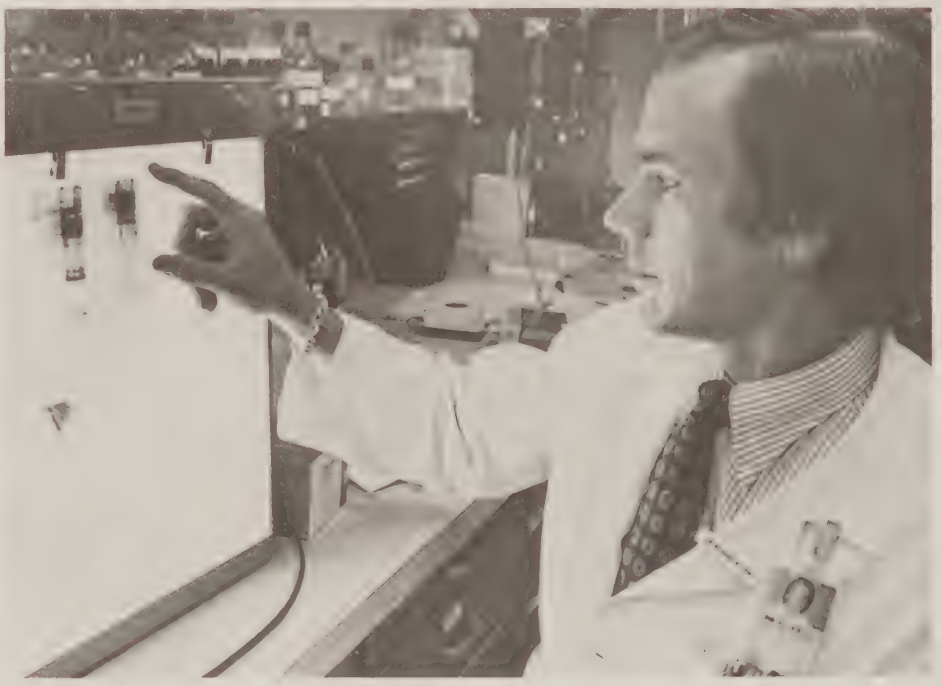
Although the tiny houses were often crowded with family members sleeping in hammocks strung across every available corner, the researchers obtained a small church and a little deserted store to use as their clinic.

In general during the stay in northwest Venezuela, the team found that the youngest people who could be diagnosed with reasonable certainty as having Huntington's disease were in their late 20s.

In a study of one family, both parents had the illness. Most of a dozen offspring submitted to examinations, and about half of them also exhibited signs of the disease.

Dr. Erbe, who is in addition Associate Professor of Pediatrics at Harvard Medical School, described the descendants of Anton Doria as quite knowledgeable about the malady that plagues them.

"The Venezuelan authorities have tried to acquaint the people with the facts," the doctor said, "and as a consequence I think the tolerance among the villagers for those with the disease is much higher than elsewhere." ■



An X ray showing a sequence of DNA from a collected specimen is examined by Dr. Richard Erbe for possible variations that might help in locating a diseased gene.

MGH News

Massachusetts General Hospital, Boston, Massachusetts

Vol. 41 No. 6 September, 1982

Magnet Draws Interest in New Diagnostic Method

Ever Ready to Treat High-Risk Injuries

"I flew up the west face of Mount Washington, soared over the summit, then headed south, keeping my eyes open for a landing site in case I had to put down, and that is the last I remember."

Harvey Howell's 15-meter (49-foot wingspan) glider traveled another 60 miles before crashing in a field at Sandwich, N.H. His flight to soar over New England's highest peak had originated only a short distance from the crash scene.

After ripping off the nose of the sailplane to extricate the 55-year-old Dover, Mass., resident, rescuers rushed him to Lakes Region General Hospital in Laconia.

So extensive were Mr. Howell's injuries that after emergency treatment an ambulance transferred him to Concord Hospital. But he did not remain there either for long. Word went out to the MGH that a critically injured patient was on the way.

What happened in the hours that followed demonstrated dramatically the kind of battle that a trauma center must be prepared to wage.

Medical authorities define trauma as a sudden, unexpected injury to one or more of the body's systems. Each year 225,000 Americans suffer injuries serious enough to place them in a high-risk category. Among children, trauma is the leading cause of death, some 16,000 fatalities being reported annually in the under-14-year age group.

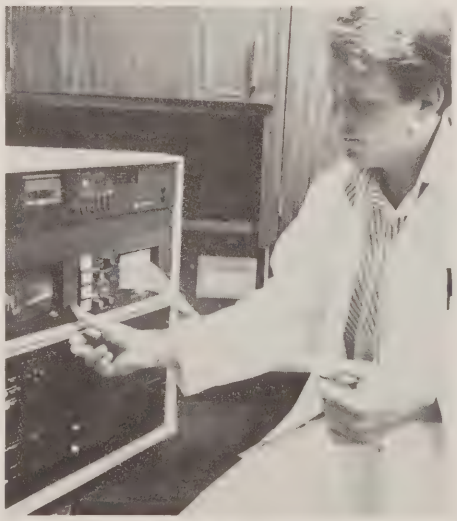
For 12 hours after his arrival at the MGH, Mr. Howell lay on an operating table as a surgical team headed by Dr. Ingrid Eriksson, Assistant in Orthopaedics, worked with rods, plates, and screws to repair more than a dozen broken bones. The team also used bone grafts in places where portions of bone were missing.

Mr. Howell's fractures included breaks in his spine, pelvis, breastbone, ribs, cheekbone, left upper arm, left elbow, left forearm, right hand, and both of his legs.

Dr. Eriksson said most of the fractures broke through the skin in the accident, and there was great concern that infection might develop.

Because of the patient's head injury, a neurosurgeon examined him shortly after his arrival, and a computed tomography (CT) scan also was taken. The scan reassured doctors that Mr.

(Continued on Page 2)



In the MGH Emergency Ward, Dr. William G. Hendren demonstrates equipment that can receive an electrocardiogram of a trauma victim from the accident scene.

The window to what goes on inside the human body is fast enlarging.

A variety of advances have resulted in a technological revolution in medical diagnosis during the past decade. (See sidebar story on page 6.)

Now, another large windowpane is being fashioned. Although still in the investigational stage, nuclear magnetic resonance (NMR) imaging holds promise of supplying pictures of how the body both looks and works.

"This is a tremendously exciting area with a great future," said Dr. W. Gerald Austen, MGH Chief of Surgical Services. "The present technology clearly demonstrates that this technique can create better images in some disease processes than presently available diagnostic techniques such as computed tomography [CT] scans.

"In addition, there is a great advantage in not subjecting the patient to X rays. In areas such as cardiac diagnosis, NMR appears promising in the evaluation of a number of abnormalities; there is really no comparable CT scan application. Further, since NMR can define metabolic changes, this may be a unique aspect of NMR application."

While many other diagnostic methods expose patients to radiation or injections, NMR testing requires only that an individual be placed in a magnet and that a predetermined radio signal be beamed at the body area under study.

The signal excites or energizes atoms (in the MGH studies, hydrogen atoms), causing them to emit signals of their own. A computer fashions these into a three-dimensional image of the target area and also provides information

(Continued on Page 4)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
J. Robert Buchanan, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIAL:

An Exciting Potential for a New Tool

When the CT scan became reality a decade ago, some scientists called the device the greatest radiologic advance since Roentgen discovered the X ray. In the minds of many, experience since then has confirmed this evaluation. For neurologists, neurosurgeons, neuroradiologists, and to some extent psychiatrists, practicing their specialties without the CT scan would be like facing a Rich Gossage fast ball with a twig instead of a baseball bat.

It took more than 75 years to go from the first X-ray device to CT. Less than 10 years later a non-X-ray instrument called Nuclear Magnetic Resonance (NMR) has emerged. This new procedure, described in a page 1 article, stands at relatively the same stage now that CT did when the MGH performed studies with the second such device in North America. Researchers at the MGH, which helped pioneer in the development of NMR, are excited. As scientists they know, however, that much evaluation lies ahead. Yet, even now it is clear that NMR can offer some diagnostic clues that CT misses. That is the conservative viewpoint.

The unproven radical one is that in a few years NMR's capabilities will dwarf those of CT. One of the more exciting aspects is that NMR makes it possible to observe in three dimensions rather than two how tissues are functioning. In the future it may even be possible for the first time to see how some chemical processes function within the body in sickness and in health.

The MGH is planning to acquire a whole body scanner. Since the hospital will use the unit for a series of studies, the MGH will not charge these patients for their diagnostic tests.

By carefully evaluating the device, investigators here and at two or three other centers around the country would like to determine the most effective ways to use NMR for the maximum benefit of patients and the least cost. The result could well be a leap forward in health care.

As with any major technological advance, though, NMR will exact its price. More than $1 million per machine. The potentially revolutionary nature of NMR would ordinarily cause a stampede to acquire one.

In an era of high medical costs, however, wisdom dictates a slower approach: Researchers at the MGH are carrying out a thorough appraisal to determine the strengths and weaknesses and the best applications of NMR imaging.

If the machine proves as valuable as many expect, wisdom and restraint may get left at the starting gate. That is exactly what the MGH hopes to prevent.

Severely Hurt Patient Could Need Services Of Varied Specialists

(Continued from Page 1)

Howell had escaped neurological harm.

An ophthalmology resident at neighboring Massachusetts Eye and Ear Infirmary (M.E.E.I.) was summoned to examine Mr. Howell's right eye which showed signs of possible serious injury. But the doctor found that a muscle controlling the pupil had become temporarily paralyzed due to the impact of the glider crash. The paralysis gradually abated.

Other problems arose, such as a urinary tract infection and abnormal liver function, but they were dealt with effectively.

Although he remained hospitalized for more than two months, the attention Mr. Howell received from people in numerous medical specialties guided him toward a good recovery.

"While we won't be sure for some time, we believe that he should have good use of both his arms and legs," said Dr. Eriksson, "although his left elbow and right foot may need further surgery."

As for piloting a glider again on weekend breaks from a plastics manufacturing business he operates in Manchaug, Mass., Mr. Howell said he was "thinking that over." But, he reflected, the view from above Mount Washington was "absolutely gorgeous."

Since the MGH opened its doors in 1821, the hospital has been dedicated to caring for victims of trauma. Of the first 15 operations performed by Dr. John Collins Warren, the MGH's cofounder and first surgeon, 7 were for traumatic conditions, primarily fractures or dislocations.

Because of the high incidence of trauma in the young, the MGH has given priority through the years to the development of emergency care specially suited for children.

In 1980, the Metropolitan Boston Hospital Council formally designated the MGH and M.E.E.I. as one of three Boston-based trauma centers, all fully staffed around the clock to provide comprehensive, highly skilled medical treatment for severely injured victims.

The other designated trauma centers are the Boston Emergency Medical

Photographs: Page 6, courtesy of the Journal of Computer Assisted Tomography. All others by Myron Daniels.

Harvey Howell of Dover, Mass., severely injured in glider crash, being tended by Amanda Savage, RN

Center (Boston City Hospital and University Hospital) and the Harvard–Longwood Institutions for Emergency Service (Beth Israel Hospital, Brigham and Women's Hospital, and Children's Hospital Medical Center).

The MGH–M.E.E.I. center was described by the hospital council's on-site inspection committee as not only meeting but exceeding all Level I trauma center criteria. The two institutions have for many years worked together to avoid costly duplication of services.

The American College of Surgeons suggested that a Level I center should be a metropolitan institution of more than 500 beds with approximately 1,000 admissions of seriously injured patients per year to maintain a high skill level as well as justify the costs involved. It added that trauma training programs and research are indispensable components of trauma care.

"If you look into the development of trauma treatment during the past 50 years, you find that in the early days there was very little the emergency room doctor could do for a patient if he were severely injured internally," said Dr. John F. Burke, Director of the MGH–M.E.E.I. Trauma Center. "It didn't make any difference whether one physician or five were on duty because a single individual could handle everything that could be done at the time.

"As specialties developed with effective approaches to such problems as controlling hemorrhages, treating shock, or dealing with pulmonary, kidney, or heart failure, the numbers of people caring for a patient increased. A trauma service then became important to coordinate the activities of these experts."

Dr. Earle W. Wilkins, Jr., Chief of Emergency Medical Services at the MGH and a pioneer in the establishment of trauma centers in Greater Boston, said trauma care takes precedence over every other hospital activity.

Operating rooms can be made available on a moment's notice at the MGH, he said. The White, Gray, and Jackson Buildings have a total of 31 rooms fully equipped for surgery.

At night, enough surgeons, anesthetists, and nurses are on duty to assemble five teams for simultaneous emergency operations.

Dr. Wilkins said that behind the

(Concluded on Page 4)

Wars Proved Worth Of Trauma Centers

In vast rural areas of the United States, motor vehicle accidents, although infrequent, account for more than 80 percent of the nation's highway-related deaths.

Health officials claim that more than half of the deaths could be prevented if proper medical care were available.

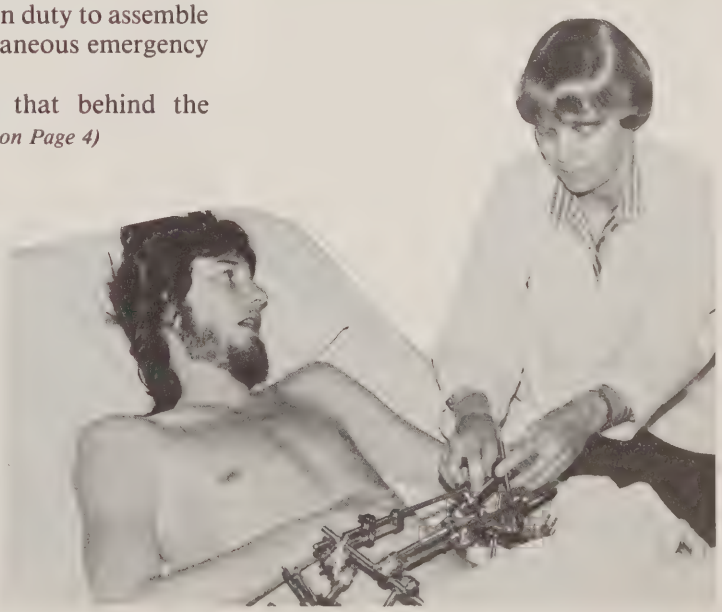
The Korean and Vietnamese conflicts demonstrated how well-trained paramedical personnel in the field, good communications, rapid transportation, and specialists in well-equipped hospitals could reduce battlefield mortality.

But the concepts and techniques which had proven themselves in war were not immediately carried over into civilian life.

Prior to 1974, Illinois and Maryland were the only two states that had established organized trauma services.

In recent years, guided by the American College of Surgeons, and supported by federal legislation and funding, numerous trauma centers have been created.

Many small community hospitals with limited medical resources now enjoy around-the-clock backup from major centers where general surgeons and surgeons of various subspecialties are available with anesthetists, nurses, and technicians to cope with trauma that may be life-threatening. ■



Dr. Ingrid Eriksson checks apparatus holding together the fractured pelvis of David Bryan of Milton, Mass., victim of a traffic accident.

Dr. Ferdinando Buonanno prepares a patient for an NMR imaging test.

Magnetic Procedure Avoids X-Ray Risks

(Continued from Page 1)

about the chemistry of the tissue in question.

Hydrogen atoms are used for the research because of their strong signal and because three-quarters of biological tissue contains water with its familiar makeup of two parts of hydrogen for each part of oxygen. What's more, the distribution of the hydrogen changes during disease or injury.

The testing procedure is painfree, and evidence to date indicates it is risk-free.

Actually, NMR is not a new concept. In the laboratory chemists have used the process for more than 30 years to analyze the structure of chemical molecules. Only in the last few years, how-

Trauma Centers

(Concluded from Page 3)

trauma teams 16 services representing as many specialties stand ready to provide whatever further expertise may be needed.

Twenty years ago last May it was an MGH Chief Resident in Surgery who led a team which performed the world's first successful replantation of a severed limb. Since then, the MGH has remained a leading center for replantation.

One of the major improvements in health care engendered by creation of the MGH-M.E.E.I. Trauma Center stems from development of more efficient communications.

Dr. Peter L. Gross, Associate Chief of MGH Emergency Medical Services, pointed out that by means of special telemetry equipment installed in the Emergency Ward (E.W.), doctors at the hospital can receive and evaluate EKGs (electrocardiograms) taken of patients still at an accident scene.

In addition to these tests of the heart's electrical activity, he said, the E.W. receives a summary of the specific medications given by paramedics attending the patient.

The E.W. also has radio facilities for use in any statewide disaster. The hookup with key public and health agencies constitutes an indispensable link in coordinating emergency medical care.

During fiscal 1980–81, more than 88,000 persons sought treatment in the MGH's E.W., and the M.E.E.I. provided emergency services to more than 39,000 individuals during a similar 12-month period. The total makes the MGH–M.E.E.I. Trauma Center the area's busiest.

Dr. Charles J. McCabe, Assistant Chief of Emergency Medical Services at the MGH, said approximately 1,800 patients are treated in the hospital's E.W. each year for major trauma.

Postgraduate training of physicians in trauma management therefore receives high priority. Dr. McCabe said that about 400 physicians come to the MGH each year for such courses given by members of the E.W.

They also join other MGH staff personnel in offering lectures under auspices of Harvard Medical School's Department of Continuing Education.

"The field of emergency medicine is expanding greatly," said Dr. Burke, who is also Chief of the MGH Burn Unit and Professor of Surgery at Harvard Medical School.

"I think trauma centers will be a major factor in assuring immediate and more effective care of injured people, and that in the long run by reducing the problem and improving functional results following injury the overall cost of health care will be less." ■

Anthony Fucaloro, Unit Manager in the MGH Emergency Ward and Overnight Ward, tests statewide radio hookup that would be used in a disaster.

With the help of a computer, Dr. Thomas Brady works with NMR scan data to construct an image of a body part.

ever, has the technology been diverted to analyze human tissue for the presence of disease.

Drs. Gerald M. Pohost and Mark R. Goldman, both MGH cardiologists, have been engaged in NMR research since 1977 in collaboration with Drs. Eric T. Fossel and Joanne Ingwall of Harvard Medical School. In 1979 NMR imaging research was instituted through a contractual agreement with the Johnson & Johnson Company's Technicare Corporation which provided the imaging equipment.

Dr. Pohost, now Director of NMR Research at the MGH, said investigators are still in the initial phases of evaluating the significance of various abnormalities that NMR detects.

"The image we obtain is a complex function of many things," he said. "Much work lies ahead to determine just what data are important for patient diagnosis."

He said NMR studies with MGH patients have dealt primarily with neurologic questions thus far because the particular imaging magnet being used cannot accommodate a study sample larger than a human head.

Drs. J. Philip Kistler and Ferdinando S. Buonanno of the MGH Neurology Service have been responsible for the NMR evaluation of some 200 patients afflicted with stroke, brain tumors, multiple sclerosis, and other neurological disorders.

The sensitivity of NMR imaging became quickly apparent.

Dr. Thomas J. Brady, who heads the hospital's clinical NMR imaging program, said NMR appears very useful in delineating low-grade tumors that infiltrate the brain. In one patient whose CT scan was negative, the NMR results were clearly positive. A biopsy later revealed a low-grade tumor called an astrocytoma.

"Computed tomography may appear normal if the changes are only at a biochemical or biophysical level," the doctor pointed out. "However, if these changes are significant, NMR may detect them."

NMR images may prove to be just what doctors have been looking for to diagnose multiple sclerosis, a disease which often defies diagnosis in its early years. MS stems from the destruction of myelin, a white, fatty material which encases and insulates nerve fibers. This so-called "white matter" in the brain appears very bright on NMR images. Consequently, patches lacking myelin show up as dark, well-circumscribed lesions, usually at multiple sites in the white matter.

"On the basis of what NMR imaging has demonstrated thus far, one cannot help but be optimistic about its future usefulness in patient care," said Dr. Joseph B. Martin, MGH Chief of Neurology. "Whether NMR will one day replace CT in diagnosing certain neurologic or other diseases, only time will tell."

The three-dimensional capability of NMR can be very important to both doctor and patient. Whereas two-dimensional CT examines one "slice" of tissue at a time from 180 different angles, NMR signals come from the whole head or whole region of the body being studied. Thousands of angles are involved.

Ian L. Pykett, Ph.D., a Technicare physicist at MGH, said that after a patient has undergone NMR testing, a computer can employ the original 3D data to calculate the signal distribution in any slice of tissue from any angle.

"A surgeon would know exactly where a tumor was, for example, because the 3D information would furnish the stereotactic coordinates," Dr. Pykett said. "To get the same data from CT, many separate pictures would be required with substantial exposure of the patient to radiation."

CT does enjoy advantages over NMR. For one thing, NMR provides no signals from compact bone whereas in computed tomography the strongest signals originate in bone. Scanning with NMR also takes much longer at present than with CT.

Obtaining data for each NMR slice requires two to four minutes compared to only 10 seconds to a minute and a quarter for a CT scan.

To carry out one complete sequence that would provide NMR images in all

(Concluded on Page 6)

The NMR Concept

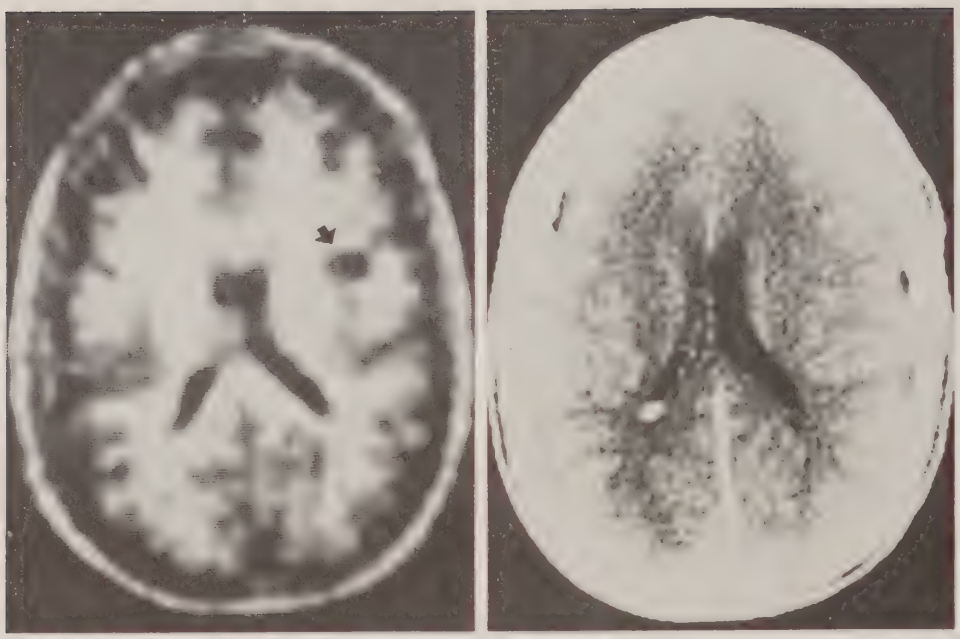
Normally the nucleus, or core, of an atom in the human body may point in any direction.

Success of NMR imaging depends on reorienting the atomic nuclei under study so that they all point in specific directions.

The alignment is accomplished by placing the patient in a magnet because it makes the nuclei follow the lines of force of the magnetic field.

A brief radio signal then beamed at the nuclei excites them, temporarily disrupting the alignment. As they come back into line, the wobbling nuclei emit signals of their own.

A computer, picking up these signals, converts them into an image of the body part. This image varies depending on the state of health of that body part. As pioneering specialists become more skilled in interpreting the picture, they broaden the scope of NMR as a diagnostic tool. ■



In left photo, arrow in NMR image points to clearly outlined tumor while a computed tomography scan of the same patient (right photo) fails to detect the growth.

Much NMR Research Lies Ahead

(Concluded from Page 5)

desired planes takes between 15 and 35 minutes.

"It can be predicted, however, that as the technology develops, the time needed to generate the data will be shorter," said Dr. Juan M. Taveras, MGH Chief of Radiology. "And while it may never become as short as a few seconds, it nevertheless will be short enough so that motion may not be a problem."

Dr. Taveras also said that one real advantage over CT may turn out to be an NMR ability to generate four or more slices simultaneously, something CT cannot do.

NMR cannot match functional information on metabolism available from a technique called positron emission tomography (PET), still in the research stage, but Dr. Pykett said, "We think that down the line NMR might hold its own in this regard."

NMR's advantages over PET include a much clearer, sharper image without any need for injections. The positron process is based on an injection of a weakly radioactive tracer chemical made by a cyclotron.

NMR testing can be carried out in several ways, each providing an independent image and requiring a separate means of interpretation.

Doctors may want to know the concentration or density of the hydrogen atoms in a certain area of the body, or they may seek what they describe as either of two relaxation times (termed T_1 and T_2).

After radiowaves excite the atoms, the point at which they begin to return to their original equilibrium represents the atomic concentration, and the times needed for the signals to decay, and for the nuclei to get back to their initial state, constitute the so-called relaxation times.

An important part of the MGH research involves trying to learn which procedure would provide the most pertinent data about specific diseases.

The MGH and the medical center of the University of California at San Francisco are the medical institutions in the United States which have been involved in NMR imaging studies for the longest time. Within the past few months other hospitals have become involved.

The MGH work gained impetus with the assistance of Waldo S. Hinshaw, Ph.D., a physicist who had been engaged in NMR work for five years at Nottingham University in England. While at Nottingham, he devised an approach to NMR imaging that produced clearer pictures than ever before possible.

After about a year at the MGH, Dr. Hinshaw transferred to Technicare in Ohio to spearhead development of the device now being tested at the MGH. He was replaced at the MGH by Dr. Pykett who had been a long-time colleague at Nottingham.

Like the early MGH investigators, Dr. Hinshaw is now looking beyond hydrogen atoms. Creating the most interest is phosphorus. In this chemical family, the compounds adenosine triphosphate and phosphocreatine sustain energy transfer processes within cells.

Dr. Hinshaw said that in current studies observing changes in these compounds in excised tissue, researchers hope to be able to determine the severity of tissue injury and the chances for recovery with intensive treatment.

"Phosphorus imaging has not yet been conducted on patients," he said. "It is in the future, but when that happens, that is where the real excitement will be." ■

An Array of Tools for Diagnosing Disease

On August 2, 1973, the MGH became only the second medical center in North America to install a computed tomography (CT) scanner, capable of X-raying human tissue to detect disease (*MGH News,* September 1974).

The ensuing years have seen a rapid-fire procession of advances in diagnostic methods.

The principles behind sonar, the World War II submarine hunter system, also led to ultrasound, extremely useful in spotting cardiac, breast, prenatal, and other abnormalities (*MGH News,* June–August 1974 and December 1979).

More recently, a new method of X-raying blood vessels—digital subtraction angiography—has appeared on the patient care scene (*MGH News,* January–February 1982). Administered on an ambulatory basis, the procedure entails less discomfort, risk, and expense than conventional angiography.

Still in the wings but of ever increasing interest is positron emission tomography (PET) (*MGH News,* April 1980). The result of studies dating from the early 1950s, including pioneering work at the MGH, PET complements the structural or anatomical images of CT by demonstrating physiologic functions, such as blood flow and oxygen or glucose metabolism. ■

Newly Opened Clinic Offers Help Against Neuromuscular Ills

Using a centrifugal analyzer, Chemistry Laboratory Technician Lisa Paci checks a blood sample for its content of an enzyme that is always higher in patients with the Duchenne form of muscular dystrophy.

To most people, muscles connote strength—power to push, pull, or lift.

They, of course, do a lot more. Without muscles, one would not be able to smile, scowl, wink, twitch, point a finger, or in fact perform the slightest kind of movement.

Dr. Raymond D. Adams, former longtime Chief of Neurology at the MGH and author of a leading textbook on muscle diseases, once spoke of the relationship between muscles and man's intellect.

"Everything man has learned and conceived," he said, "has had to be delivered to the world through mechanisms involving the spinal cord and the neuromuscular system. These neural and muscular elements working together have formed the basis of human civilization. Without the ability to move, the human organism is truly impotent."

For some 200,000 Americans suffering from any one of the neuromuscular disorders, muscles fail to provide many of the benefits that one normally takes for granted.

These diseases may affect the spinal cord, peripheral nerves, or muscles themselves. A few cause progressive crippling and sometimes even death.

Many of the muscular dystrophies and related neuromuscular disorders are inherited, but in each instance the disease-causing gene, the muscle structure involved, the way the malady spreads, and its rate of progress differ.

Recently, in collaboration with the Muscular Dystrophy Association (M.D.A.), the MGH opened a clinic for people who can receive careful diagnostic evaluation and specialized long-term follow-up for any one of 40 neuromuscular disorders.

Held every Thursday afternoon in the Ambulatory Unit of the Neurology Service, the clinic also makes available a wide range of services offered by the M.D.A.

The association pays for diagnostic and therapeutic care provided or ordered through the clinic unless already covered by other third-party agencies.

At each clinic session, patient care representatives from the association stand ready to coordinate medical attention with such home and community services as transportation, recreation, and the use of wheelchairs or other appliances.

The illnesses affecting muscular strength are quite varied. Normally, the brain controls muscles by sending impulses to the spinal cord, which in turn controls the nerves leading to the muscles.

As an example of how the disorders can differ, in myasthenia gravis (*MGH News,* September 1975), the illness which led to the death of Aristotle Onassis, the transmission of signaling impulses somehow becomes blocked at the junction of the nerve and the muscle. In amyotrophic lateral sclerosis (A.L.S. or Lou Gehrig's disease), both the brain's behavioral commands and the muscle are ready, but the link in the spinal cord is lost.

"Often it is difficult to say what is a nerve disease and what is a muscle disorder," said Dr. Dennis M.D. Landis, Director of the new clinic. "Even in laboratory settings it is not always possible to tell the conditions apart. So all are classified as neuromuscular illnesses."

Dr. Landis described the new clinic as a coming together of components which have been in place for a long time at the MGH.

"The Clinical Neurophysiology Laboratory which does electromyographic [muscle activity] studies—a key factor in understanding neuromuscular diseases—is among the very best in the country," he said.

"In terms of physician expertise, we have such specialists as Dr. Raymond Adams, who was one of the first to write a book devoted to the diseases of muscle, and Dr. Vincent Perlo, who may well have more personal experience in dealing with myasthenia gravis than anybody in America. The new clinic will complement a myasthenia gravis clinic conducted by Dr. Perlo."

Dr. Landis also directs the MGH's Neurocytology Laboratory. With the help of an electron microscope, he is able to study the structure of nerves and muscles and notice any changes that may be taking place.

The most common form of muscular dystrophy—and also the most devastating—is Duchenne dystrophy, named after a French physician who first described the illness in 1861.

The Duchenne gene usually is inherited by boys from their mothers, who are carriers rather than victims of the disease. The mothers' protection arises from the fact that the genetic defect is on their sex, or X, chromosome. Women have two X chromosomes. The normal one apparently prevents the deleterious influence of the Duchenne gene on the other X chromosome.

A daughter, having two X chromosomes, is similarly protected, but she too might pass on the gene to a son of her own.

It is possible for Duchenne dystrophy to occur without any family history of the illness. The genetic defect can arise spontaneously in the mother or in the affected child.

Duchenne dystrophy usually presents initial symptoms when a child is between 2 and 6 years old. The youngster waddles or walks on his toes, falling frequently and having difficulty getting up. Muscle-wasting spreads so

(Concluded on Page 8)

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Neuromuscular Patients Learn How to Cope

(Concluded from Page 7)

that by age 12 the patient needs a wheelchair. Death commonly occurs before 20 years of age, often because of a respiratory infection.

Levels of the enzyme creatine phosphokinase (CPK) are always higher in the blood of patients with Duchenne dystrophy. The enzyme is a normal constituent of muscle but apparently leaks out of the dystrophic muscle.

In addition to confirming the diagnosis of Duchenne dystrophy, an assay of blood CPK may also help to detect carriers of the gene. Often mothers and sisters of the affected boys are found to have slightly abnormal CPK levels and so are likely to be carrying the gene.

A second, less common, form of dystrophy is facioscapulohumeral (face-shoulder-and upper arms) dystrophy. Usually appearing first in the teens, this condition can affect either sex and may progress so slowly that life expectancy remains normal. The patient's background usually reveals a strong family history of the disorder.

Both males and females can also inherit limb-girdle muscular dystrophy. Striking older children or adults in their 20s or 30s, this disease first affects either the shoulder muscles or the muscles of the lower trunk and upper legs. The face is not involved. Most patients become severely disabled by middle age, with lifespan shortened.

Still another dystrophy likely to be encountered in the new MGH clinic is myotonic dystrophy, a condition arising in early adulthood and affecting either sex. A stiffness of the hands and feet, a facial weakness such as a dropping of the jaw or eyelids, and difficulty relaxing a handshake or other grip are common symptoms. Severe disability ultimately sets in.

For some unknown reason, the disorders affecting muscles strike only at the voluntary muscles, those which the individual consciously controls. Heart muscle and "smooth" muscle in arteries or in the walls of the digestive tract are usually unaffected.

"There is very little we can do to alter the course of many of the neuromuscular diseases, including muscular dystrophy," said Dr. Landis, who is also Assistant Professor of Neurology at Harvard Medical School, "but in terms of helping someone cope with what he's got, we can do a lot."

These measures include instructing patients on how to walk when certain muscles are weak, thus keeping them out of wheelchairs, and prescribing surgical procedures that can also help improve body movement.

In addition to underwriting care to thousands of people with neuromuscular maladies at more than 230 clinics nationwide, the Muscular Dystrophy Association, founded 32 years ago, also supports a worldwide research program aimed at revealing more about these disorders.

Working under one such research grant, James F. Gusella, Ph.D., an MGH geneticist, is striving to isolate the gene responsible for Duchenne dystrophy.

By studying sequences of DNA (deoxyribonucleic acid), the chief chemical component of genes, he hopes to find a genetic marker that is inherited with the dystrophy gene and to specify its location on the sex-linked X chromosome. Strategies could then be devised to separate the gene itself for study.

Dr. Thomas P. Stossel, Chief of the Hematology–Oncology Unit in the MGH Department of Medicine, is probing a theory that muscular dystrophy accelerates a breakdown of muscle protein. He is also looking into some evidence that nonmuscle cells, such as those of the liver or other organs, may be abnormal in muscular dystrophy.

Another MGH researcher, Dr. John Gergely of the Neurology Service, is studying the role muscle proteins play in contraction and relaxation. He and his colleagues also compare normal and dystrophic proteins to determine any differences in their corresponding properties. Dr. Gergely's work is conducted at the Boston Biomedical Research Institute.

Ever since establishment of the Muscular Dystrophy Association, its driving force has been a conviction that there are no incurable diseases, only diseases for which no treatments have yet been found. ■

Dr. Robert Brown tests the reflexes of a patient in the MGH Muscular Dystrophy Clinic as Dr. Dennis Landis, clinic director, looks on.

MGH News

Massachusetts General Hospital, Boston, Massachusetts

Vol. 41 No. 7 October, 1982

New Biological Weapon May Fill Variety of Roles

Harvard Anniversary Provides a Reminder Of Links With MGH

Harvard Medical School, considered by many as America's premier educational establishment for physicians, has swung into its third century.

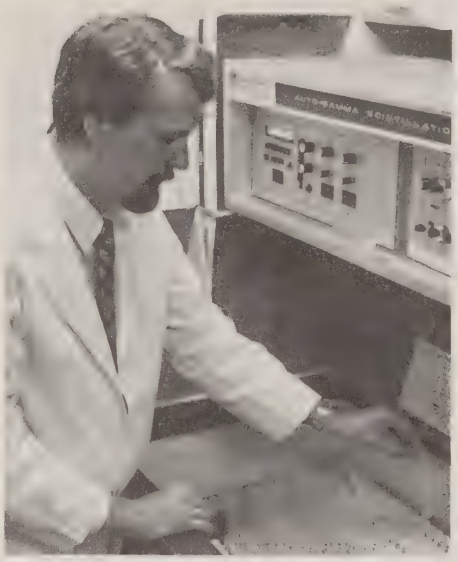
At the MGH, the milestone is being observed with a deep sense of personal pride, for much of what the school and the hospital have contributed to the advancement of medicine resulted from an interaction between the two institutions. They literally grew up together.

Harvard Medical School came into being in 1782 in modest fashion. The first lectures were presented in the basement of Harvard Hall on the Cambridge campus. Two students comprised the first graduating class in 1788. During the ensuing 25 years, no graduating group numbered more than five individuals.

In 1810 two of the school's original faculty members circulated a letter among Boston's more affluent citizens. Drs. John Collins Warren and James Jackson sought financial backing for construction of a general hospital in the city. They cited two reasons: The hospital would afford relief and comfort to thousands of the sick and miserable, and a general hospital is indispensable in the teaching of medicine.

"On what other objects can the superfluities of the rich be so well bestowed?" the doctors asked.

The appeal resulted in the establishment of the MGH, the charter being awarded in 1811 and the hospital's first structure, the Bulfinch Building, opening its doors in 1821 (*MGH News,* October 1978).



Dr. Jack Wands uses monoclonal antibodies to test for hepatitis-B virus.

Drs. Warren and Jackson became the MGH's first surgeon and physician, respectively.

Of 19 men who have become Dean of Harvard Medical School, Dr. Warren was first, serving from 1816–1817 and again from 1821–1826. Dr. Jackson succeeded Dr. Warren in 1817, serving for one year.

Fourteen of the deans were also staff members of the MGH. The latest, Dr. Robert H. Ebert, was MGH Chief of Medical Services when he was appointed Dean at Harvard, a post he held from 1965–1977.

Only two years after the hospital opened, the Harvard medical faculty issued a circular applauding the benefits that students were deriving from the new institution.

"The wards of the medical department have always furnished a succes-

(Continued on Page 2)

"It's like switching from a shotgun blast to the precision of a rifle bullet," said an MGH researcher.

When foreign organisms such as bacteria or viruses penetrate the body, its immune system responds by dispatching antibodies to destroy the invaders. Many types of antibodies may appear at once.

On its cell surface, for example, a virus can have several unique characteristics (antigens), each attracting a different antibody. But only one of the antibodies may be critical to the life of the cell.

To a large degree, therefore, the body's natural immune response is nonspecific.

Today, however, in a growing number of laboratories around the world, including several at the MGH, scientists are producing antibodies that are not only specific but also easily reproducible in uniformly pure fashion.

Called monoclonal antibodies (MAs), these invisible bits of protein appear to have the potential of serving in many ways: as germ fighters, in helping to diagnose disease, in searching out drugs to alter their effects, assisting in prevention of organ transplant rejections, and facilitating development of vaccines.

MAs can even function as guided missiles, zeroing in on targets while piggybacking payloads designed to perform certain tasks. Scientists hope one day to use MAs as carriers of powerful drugs or poisons that would seek out and destroy cancer cells. Because of their specificity, the MAs would not affect surrounding, normal cells.

To produce MAs, investigators first inject into a mouse the particular

(Continued on Page 4)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
J. Robert Buchanan, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIALS:

An Awesome Sound With Punch to Match

Monoclonal antibodies. The very name sounds awesome. In fact that is why the *News* inaugurates in this issue the abbreviation MAs. Remember those initials well. For MAs promise to make medicine—now part art, part science—more of a science. Their specificity will enable doctors to increasingly diagnose disease earlier and with even greater accuracy. And by targeting a diseased area and only that area, they will be able to root out the problem without involving healthy tissue. This potentially means chemotherapy that destroys cancer without adverse side effects to the patient. Or arthritis drugs that attack inflammation while leaving untouched the rest of the body.

With a little imagination the mind can conjure up a thousand and one treatments employing MAs. In fact therein lies a problem. The potential is so great that it is difficult to restrain one's fancy. Yet restraint is exactly what is required. As a page 1 article indicates, MAs have already made inroads on disease. But converting theory to practice is a tedious, time-consuming pursuit. Decades may pass before scientists reap many of the benefits, although some are already beginning to appear. In the meantime, however, MAs should be a reservoir of hope.

Hands Across the Ages

One arose from the Revolutionary War era. The other barely preceded the War of 1812. Harvard Medical School was born in time to serve a new nation. Massachusetts General Hospital ushered in the era of the Industrial Revolution. Through most of the nation's history the medical school and the hospital have complemented each other. In so doing, they have served the public much better than either could have done alone. For from their relationship has emerged a number of contributions, some well-known, others less tangible.

As Harvard Medical School enters its third century, the MGH looks forward to sharing the next hundred years with what many consider America's premier medical educational establishment.

Harvard Medical's Needs Influenced Move to Boston

(Continued from Page 1)

sion of interesting cases, both acute and chronic," the circular stated. "Regular clinical lectures during the winter are given upon these cases, and students are admitted to the patients so far as to become experimentally conversant with the symptoms of their diseases, the progressive changes which take place, and the operation and influence of medicinal agents."

The faculty added that "no other kind of institution affords equal opportunities for acquiring a practical acquaintance with operative surgery. Not only the operations themselves, but the treatment of the cases preparatory and consequent to the operation, and the progress and management of convalescence, may be here studied and observed."

During the fund raising for the hospital, its original construction, and its expansion over the years to more than 13 acres on or near the Charles River waterfront, Harvard Medical School occupied a succession of homes.

Drs. Warren and Jackson had predicted that the medical school would one day move to Boston from across the river in neighboring Cambridge because patients, practitioners, and preceptors were nearly all in Boston.

The school first moved in 1810 to a building at 400 Washington Street in downtown Boston. After six years, classes switched to a new structure on nearby Mason Street. Then, in 1847, the school established its base on North Grove Street, in a building situated next to the MGH's Bulfinch Building. Here the school operated for the next 36 years.

Eventually its needs called for larger quarters. A building at the corner of Boylston and Exeter Streets, near Copley Square, met those requirements in 1883. But only a few years passed before medical education once again demanded larger space.

The next move was to the school's present site. Twenty-five acres of land

---

Photographs: Pages 1, 5 (upper), 6, 7, Myron Daniels; p. 3 (upper), MGH Archives; p. 3 (lower), courtesy of Harvard Medical School; p. 5 (lower), Chris Maynard; p. 8, Michael Elio.

Drawings: Page 4, courtesy of Dr. Edgar Haber; p. 6, MGH Medical Art Department.

From 1847 until 1883, Harvard Medical School occupied a building (at right in photo) which stood next to the MGH's Bulfinch Building. The Charles River came virtually to their doorsteps in those days.

were acquired on Longwood Avenue in Roxbury. On it rose the present quadrangle of five imposing marble structures. A $5 million building fund which led to the dedication in 1906 was paced by gifts of $1 million or more from J. P. Morgan and John D. Rockefeller.

Throughout the developing years of Harvard Medical School and its first teaching hospital, the MGH, the achievements of doctors holding appointments on both staffs further cemented the respect and reliance that the institutions share.

Each October, the MGH holds "Ether Day" ceremonies to commemorate the most dramatic event in the career of Dr. John Collins Warren. On the morning of October 16, 1846, in an amphitheater of the Bulfinch Building, the Harvard Professor of Anatomy and Surgery and son of Dr. John Warren, a cofounder of the medical school, unveiled to mankind the benefits of anesthesia for patients having surgery.

Calling the discovery a priceless gift to humanity, Dr. Oliver Wendell Holmes, an MGH physician, coined the word anesthesia to describe the technique.

Dr. Holmes was a gifted and innovative teacher of anatomy and physiology at Harvard for 35 years. He was assigned a 1 p.m. lecture time because, it was asserted, no one else "could hold the attention or keep awake the tired and restless students in their fifth hour of classes for the day."

In the same year that Dr. Warren conducted his historic ether demonstration, James Jackson Putnam was born. He graduated from Harvard Medical School 24 years later, lectured there on nervous diseases two years after graduation, and in 1893 recorded a dual achievement. He became Harvard's first professor of diseases of the nervous system and also established the MGH's Neurology Service, acclaimed today as one of the country's finest units of its kind.

Another pioneer at Harvard and the MGH was Dr. James Clarke White. In 1871, the medical school appointed him as a professor of diseases of the skin, the first such professorship in this country. He also founded the MGH Department of Dermatology.

Dr. White's son, Dr. Charles J. White, later served as Chief of Dermatology at the hospital, and a grandson and namesake was the institution's Chief of Neurosurgery for 20 years.

In 1886, the field of surgical instruction gained strides because of the work of an MGH pathologist, Dr. Reginald H. Fitz. He recognized and described the true nature of the appendix and argued convincingly that removal of an inflamed appendix could prove lifesaving by avoiding peritonitis.

In those days, surgeons loathed having to open an abdomen because of the threat of infection. Dr. Fitz's arguments lifted the curtain to the entire field of abdominal surgery.

It was Dr. Fitz who coined the word appendicitis. He said he preferred that to "Fitz's disease."

Dr. Richard C. Cabot, who in 1905 established at the MGH the first social service department in any hospital, also was credited with devising medical study programs known as clinical pathological conferences (CPCs).

The programs consisted of discussions of cases culled from difficult patient care problems for which the diagnosis was established in the MGH's Pathology Department.

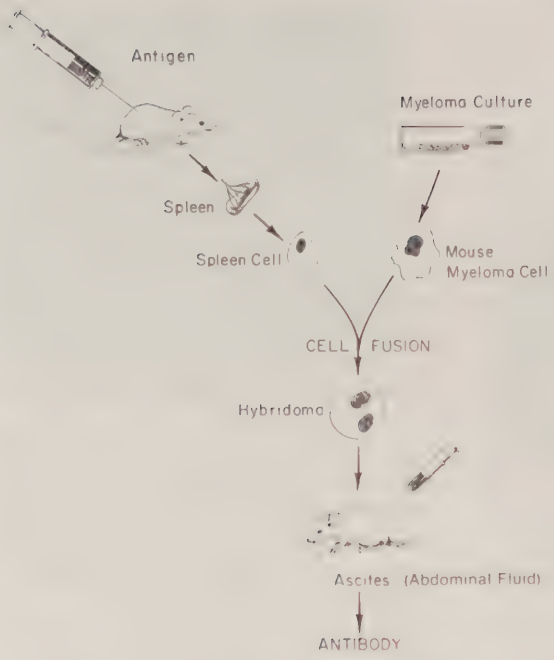
Beginning in 1895, Dr. Cabot used printed histories of patients in connection with quizzes he gave his Harvard students. The medical school formally adopted this "case method" after a few years.

In 1924, the *New England Journal of Medicine* began publishing the CPCs weekly as "Case Records of the Massachusetts General Hospital."

The late Dr. Benjamin Castleman, former MGH Chief of Pathology and Acting General Director, served as Editor of the "Case Records" for 23 years and also enabled more than 200 hospitals, medical schools, and other institutions worldwide to subscribe for CPCs as teaching aids.

(Concluded on Page 4)

Present campus of Harvard Medical School in Boston



This diagram demonstrates step by step the events that take place to make a monoclonal antibody.

MGH Conducted Early Antibody Studies

(Continued from Page 1)

foreign substance against which antibodies are sought. The animal produces its own antibodies against the substance. Then the antibody-producing cells are removed from the mouse's spleen and fused to rapidly dividing cancer cells (myelomas). The resulting cloned hybrid cells, called hybridomas, make the MAs.

The mouse cells determine the specific nature of the MAs that the hybridomas make while the myelomas assure indefinite continued growth.

The term monoclonal simply refers to the fact that each such type of antibody represents the product of a single clone of identical cells.

It was in 1963 that the MGH Cardiac Unit, which works extensively with MAs, first became interested in antibodies as a tool in cardiovascular research. That was a dozen years before Drs. Georges Köhler and Cesar Millstein of the Medical Research Council Laboratory in Cambridge, England, developed the fusion technique by which MAs are now made.

Using antibodies, the Cardiac Unit in the late 1960s devised the first practical method for measuring blood levels of the heart drug digitalis.

"Even in those early days," said Dr. Edgar Haber, Chief of the Unit, "it occurred to us that if an antibody could be helpful in measuring the concentration of a substance, the same protein might also be useful in treating patients."

Subsequently, Dr. Haber and his team showed that, after undergoing special purification, fragments of conventional, or polyclonal, antibodies could reverse toxic overdoses of digoxin, a form of digitalis.

Digoxin is such a sensitive drug that the margin between a prescribed therapeutic dose and a toxic overdose can be very narrow.

Illustrating the value of digoxin-specific polyclonal antibodies, Dr. Haber told of a 39-year-old man who took 90 times the normal daily dose of the drug. After he was hospitalized, his heart rate slowed to 10 beats per minute, and his blood potassium levels bordered on fatal concentrations. Only 10 minutes after the patient received a dose of antibody proportional to the amount of digoxin taken, his heart rate rose to 80 beats per minute, and within 5 hours his potassium had returned to normal.

In another instance, a 2½-year-old child gulped a large amount of his grandfather's digoxin, and the youngster's heart began to falter. *For 2½ hours doctors performed CPR (cardiopulmonary resuscitation) until the antibody could be injected. A half hour after receiving it, the child was sitting up asking for his mother.*

Twenty medical centers throughout the United States, including the MGH, are studying the value of antibodies for digoxin reversal. At the MGH and some other of these centers, the work involves monoclonals as well as polyclonals.

Dr. Haber, who is Higgins Professor of Medicine at Harvard Medical School, and an associate in his unit, Ban-An Khaw, Ph.D., also are directing a team in developing MAs as a tool in diagnosing a heart attack and pinpointing the damaged area.

The group uses antibodies specific for myosin, a protein in heart cells which causes their contraction during the organ's pumping process.

Normally, a membrane surrounds the cells, isolating myosin from the blood. But in a heart attack the mem-

Harvard Medical School

(Concluded from Page 3)

Dr. Castleman died in July at the age of 76 only a few weeks after Harvard had announced that Dr. Robert T. McCluskey would serve as the first Benjamin Castleman Professor of Pathology, an endowed chair at the medical school. Dr. McCluskey succeeded Dr. Castleman as MGH Chief of Pathology on his retirement in 1974.

MGHers hold 16 endowed chairs at the medical school, and the MGH recipients of two other such professorships remain to be designated.

One of the two will be the recipient of the Joseph and Rose Kennedy Professorship in Child Neurology and Mental Retardation at the MGH. The Joseph P. Kennedy, Jr., Foundation announced in July that it is giving $750,000 and Harvard Medical School $250,000 to establish the chair.

Speaking at a celebration of his mother's 92nd birthday, Senator Edward Kennedy said:

"We would hope as a result of the establishment of this professorship that there would be more information available to families, not only here in Massachusetts but across the country, on how mental retardation can be prevented, what the causes are for mental retardation, and the best opportunity for medical treatment in the future."

The Kennedy family had previously established the Joseph P. Kennedy, Jr., Memorial Laboratories at the MGH.

As Harvard Medical School observes its anniversary, numerous MGH departments are arranging activities to help commemorate the occasion and the new era that is beginning. ■

brane is damaged, and the protein becomes exposed.

Drs. Haber and Khaw found that not only would myosin-specific antibodies attach to the exposed myosin, verifying the heart attack, but if the antibodies were tagged with a weakly radioactive chemical, a type of nuclear camera (gamma) could also form an image of the chemical, delineating the site of the attack.

After extensive laboratory studies, the first patient care trials of the diagnostic technique are under way.

The Cardiac Unit is working with animal models to assess the role MAs might play in the treatment of high blood pressure. Renin, a kidney enzyme, initiates a reaction which can alter blood pressure. Several agents demonstrated that they can interrupt this reaction, but they also disturbed additional systems. MAs, on the other hand, inhibited renin without affecting any other parts of the body.

Still in its embryonic stage is a project to determine whether MAs can serve as so-called beta blockers to treat conditions such as pain coming from the heart (angina pectoris).

Beta blockers slow the heart and ease its workload creating less need for oxygen. But these drugs are nonspecific. While benefiting the heart, they may also block in the lungs beta receptors which keep air sacs open. If a patient with asthma took a beta blocker, the asthma might worsen.

Dr. Haber said a colleague, Dr. Charles Homcy, has shown that MAs can differentiate between receptors in the heart and those in the lungs.

In making a monoclonal antibody, Dr. Charles Homcy first uses a laser-equipped device to select cells most antagonistic to the substance being suppressed.

In the MGH Gastrointestinal Unit, researchers have included MAs in developing a new, more sensitive test to detect hepatitis-B, a viral infection of the liver. The disease, which affects some 200 million people around the world, may be transmitted through blood transfusions, close interpersonal contacts, or poor hygiene.

The MGH assay is undergoing extensive patient care trials at this hospital and four other centers. Dr. Jack R. Wands, the principal investigator in the GI Unit, said that "while the data we have thus far are preliminary, they nevertheless support our belief that the test is highly sensitive and specific for hepatitis-B."

Dr. Wands said that MAs can find viruses circulating in the body when their presence is missed by conventional tests.

"The important public health aspect of the new assay is its value in the screening of blood donors," said Dr. Kurt J. Isselbacher, Chief of the GI Unit. "There's always some small risk in transfusions. Anything we could do to reduce the risk of hepatitis associated with transfusion would be significant."

MAs also have found a place in the care of kidney transplant patients at the MGH. In pioneering studies the antibodies have proved efficient both in monitoring patients for early signs of transplant rejection and in treatment after rejection had actually begun.

To protect a transplanted kidney, the patient's immune system, or defenses against foreign matter, must be suppressed with drugs. In the past, a major problem has been inability to assess levels of immunosuppression in the bloodstream. A high level might leave the patient a prey to infection, while too little could lead to rejection of the new organ.

MAs enable doctors to determine the amount of suppression remaining at any given time. "We now routinely monitor our transplant patients two to three days a week with monoclonal antibodies, and we change their immunosuppressive drugs on the basis of what we find," said Dr. A. Benedict Cosimi, Chief of MGH Transplantation Surgery.

In countering rejection, MAs attack

(Concluded on Page 6)

Dr. A. Benedict Cosimi examines a kidney transplant patient whose condition has also been monitored with monoclonal antibodies.

Dr. J. Scott Rutan in a psychotherapy session

Choosing the Setting for Psychotherapy

Depression, fear, anxiety, hopelessness, lack of self-direction. . . . The psychological problems that can beset the human mind are boundless.

Emotional upheavals of one sort or another occur naturally in life. But when the ups and downs persist beyond a reasonable time and dominate the course of one's life, professional help may be needed to get back on track.

More than 34 million Americans receive formal counseling or psychotherapy (treatment by oral communication that may embrace suggestion, persuasion, reeducation, or reassurance).

Upon meeting a patient, the therapist, as one of his first duties, must determine the treatment setting most suited to the individual and his type of problem.

Would the patient benefit most by individual therapy, group therapy, or a combination of the two? Each has its merits but also, when adopted inappropriately, certain hazards.

Psychotherapy was traditionally employed on a one-to-one basis until World War II when psychiatrists and psychologists suddenly found themselves dramatically overtaxed. Group therapy then seemed the logical solution. The idea of combining the two types of treatment (conjoined therapy) to derive benefits from each arose only about 10 years ago.

Speaking recently at an MGH medical meeting (Psychiatric Grand Rounds), J. Scott Rutan, Ph.D., an MGH psychologist, discussed the need to understand the options in treating psychotherapy patients.

(A paper on the same subject, coauthored by Dr. Rutan and an MGH colleague, Anne Alonso, Ph.D., also appeared in the July issue of the *International Journal of Group Psychotherapy*.)

The basis for the distress bringing an individual to psychotherapy often guides the care giver in prescribing specific treatment. "If a person's unhappiness is largely rooted in who he is and how he feels about himself," Dr. Rutan said, "I would think about starting treatment on an individual basis. If, however, the unhappiness is associated with a sense of estrangement from other human beings, I would turn to group therapy."

Dr. Rutan agreed that if one feels bad about himself, chances are he will also experience difficulty dealing with others. "You have to look at where the weightedness is," the psychologist stated. "Where does the patient himself think his problem lies?"

Dr. Rutan told of a patient who had a retarded sister. As a child the patient saw his sister receive most of their parents' attention. To grab some of the spotlight and also counter depression over a sense of what he himself was, he unexpectedly acted out roles of various kinds.

"Group therapy would have been a waste of his time and money because he would have simply continued entertaining," Dr. Rutan remarked. "In individual therapy, when the patient realized I had little interest in his role-playing, he became anxious and began talking about his true feelings."

Therapy brought out in the man a realization that it was not something wrong with him but something right which figured in the shift of his parents' attention. He did not need the

Monoclonal Antibodies

(Concluded from Page 5)

a group of white blood cells (lymphocytes) emanating from the thymus gland. The cells, called "T-lymphocytes," are known to play a key part in the body's response to foreign tissue.

Dr. Cosimi said the antibodies now being used affect all T-cells. "We'd like to see a more selective monoclonal," he said, "one that will deal only with a specific subpopulation of T-cells, the one most intimately involved with rejection. I think that we'll be down to a subset of T-cells within several years."

As work toward this goal goes on, MGH doctors, using MAs, have seen the survival rate for transplanted kidneys at the hospital increase from 60 percent to nearly 80 percent. ■

In contrast to the shotgun-like approach of conventional antibodies, the action of monoclonals has the directness of a rifle bullet.

Young Tennis Player Winning Long Fight Against Leukemia

Score another win for 16-year-old Terry Elio, one of the brightest young stars on the New England tennis scene.

For the past three years while earning tennis accolades, including selection as a member of the *Boston Globe's* 1982 All-Scholastic Team, Terry has also been competing against leukemia.

Recently, the Winchester High School student received her final treatment from Dr. John T. Truman, Chief of the Pediatric Hematology–Oncology Unit at the MGH.

While insufficient time has passed to proclaim a cure, the only medication that Terry takes today is an antibiotic (bactrim) in sharp contrast to the daily regimen of five drugs (26 pills) once

(Concluded on Page 8)

As her mother looks on, Terry Elio receives her final anticancer shot from Dr. John Truman.

adoration that his sister did.

Once his depression ended and he was able to let people know him as he never could before, the man continued to use his performing skills by presenting shows at a hospital for the retarded.

Dr. Rutan cited an instance in which group therapy was clearly the choice. The patient was a young man who during his childhood had experienced merciless private beatings by his father.

"The son had a lot of issues to resolve, but he wasn't about to sit alone with me for fear of a physical confrontation," the doctor said. "In his case, a group represented a number of chaperones, protectors if you will, sitting around to make sure that whatever had to be dealt with would be aired in public."

In group therapy, members must accept the notion of sharing fairly but not necessarily equally in a session's activities. Those needing greater attention usually get it. A patient faces no such dilemma in individual therapy.

If a patient's needs clearly require a close, very trusting relationship with the care giver, then a one-to-one association with the therapist is a must. Severely borderline patients, for example, often become so possessive of the leader that if they were in a group they would be unable to tolerate the specter of his interest being directed to others. Such a situation could not only cause heartache but regression of the patient's condition and even destruction of the group.

This is not to say, however, that a patient requiring individual therapy cannot in time move into a group.

For instance, an individual too frightened to be with other people could gradually build up self-confidence by meeting alone with the therapist. At the point where the patient has mustered enough courage to at least sit with others and hear their thoughts, the transfer would take place, or the therapy would become a combined one.

Dr. Rutan, who is Clinical Instructor in Psychology at Harvard Medical School, said people who feel their struggle is unique often are helped very quickly when they find others going through the same dilemma.

"Chances are 90 out of 100," he said, "that when a person enrolls in a group he discovers that some members are just beginning their treatment, others are halfway through the process, and some are nearly finished. So the newcomers can learn right away what the prospects are for success of the therapy."

Groups exist indefinitely, although members come and go. The average length of stay in a group, usually numbering between six and ten members, is two or three years. Individual therapy may range longer or shorter. Patients typically meet weekly with the therapist regardless of the setting.

The value of conjoined therapy has been debated at length. Some professionals regard individual and group therapy as different kinds of treatment which should not be mixed. Also, they argue, if a therapist saw the same patient both alone and in a group, preferential attention might be given in the group.

Dr. Rutan said, however, that in his experience conjoined therapy has provided extraordinarily rich opportunities for care giving.

Observing the patient in two different contexts enables the psychologist or psychiatrist to obtain a much more realistic picture of the troubled person.

Dr. Rutan said the therapist often is amazed by differences in character and methods of coping adopted by the patient in the two settings. The stereoscopic view, he said, creates a much better data base for use by the patient and therapist alike in their working relationship.

Since circumstances do not always permit one leader for conjoined therapy, Dr. Rutan stressed the importance of collaboration between those who do become involved with the same patient. No bond of confidentiality should exist between the patient and the leader of either modality, he said.

He added that the patient should not even be allowed to keep secrets from fellow members in a group. Although it might be argued, he said, that such a posture can endanger the patient's sense of trust and safety, anything short of total openness might raise barriers to the individual's understanding of his problem and how it might be solved. ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

She Starred in Tennis Despite Leukemia

(Concluded from Page 7)

prescribed.

"The antibiotic will give Terry a bit of extra protection during the next couple of months," Dr. Truman said. "After that, she will be off drugs completely."

The youngster will continue to visit Dr. Truman's office for blood checkups, at first monthly for a year, then bimonthly during the second year, and quarterly in the third.

"The chance of the disease recurring at that point would be very slim, probably less than 10 percent," the doctor said. "If seven years after diagnosis there is no longer any sign of the disease, Terry will be considered cured."

She was stricken with acute lymphocytic leukemia, a cancer of blood-forming organs which induces lymphocytes, a type of protective white cell, to proliferate abnormally.

Her first encounter with the illness took place in August 1979 when she suddenly developed severe leg cramps while competing in a tennis tournament at Yale. Since the weather was damp and chilly, doctors dismissed the attack as probably due to the poor playing conditions.

"I swam and was given leg massages, but nothing seemed to help," Terry said. "After returning home, some medicine a doctor gave me eased the pain, but later I got cramps in my arms."

The Elios' family physician examined the girl, found her red blood cell count to be low, and on August 30, 1979, referred her to Dr. Truman. He tested not only her blood but also her bone marrow, the production area for blood.

"Sometimes when leukemic cells are being produced, they are not delivered to the blood, so you have to go looking for them," he said. "Bone marrow really tells what is going on. The blood is only the tip of the iceberg. The bone marrow is the iceberg."

Upon the diagnosis of leukemia, Terry, then a 13-year-old eighth grader, began a program of intensive chemotherapy. After five days of hospitalization, she went on a daily battery of pills that included:

The anticancer drugs prednisone and dexamethasone,

Allopurinol to make sure her kidneys could dispose of all the destroyed disease cells,

Cimetidine to prevent a possible stomach ulcer,

And colace to guard against constipation.

After four weeks on this schedule, Terry visited the hospital daily for 10 days to receive injections of the anticancer drug asparaginase. Then came a series of radiation treatments and spinal shots, using the drug methotrexate, to kill any leukemic cells that might be lurking in her brain or spinal cord.

Although the cancer was in remission after only the first month of treatment, Terry missed 50 days of school, but her town provided a tutor (and the youngster wound up the school year with straight A's). Dr. Truman ruled out tennis temporarily for fear the teen-ager might bruise herself.

In April 1980, just eight months after her treatment began, Terry was back at the game with the doctor's approval. "I had to regain my timing and coordination," she said, "but I was determined to get back what had been taken from me."

In the ninth grade (1980–81), Terry played on a tennis team that advanced to the semifinals of the state championship. During the past school year as a sophomore, in addition to the *Boston Globe* honors, she and a partner made the Middlesex County League's All-Star Team and were also voted best athletes by a local newspaper, the *Woburn Daily Times.*

Terry attributes much of her success in life to a philosophy handed down by her father, Carmen Elio:

"He told me that if I did well both academically and in a sport I could be sure that life would be fun." ■

Terry Elio at practice

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 41 No. 8 November, 1982

Understanding an Illness by Catching One's Breath

Do the Head Sinuses Serve a Purpose?

Whenever Harvard Anatomy Professor Farish Jenkins, Jr., meets with a new group of medical students, someone inevitably asks him, "What is the function of the sinuses in the head?"

"And I'm never sure how to respond," said Dr. Jenkins, "because no one really knows the answer. One might think all the sinuses do is cause trouble."

Millions of Americans know the discomfort that can occur when one or more of these open spaces surrounding the nose is plagued by an allergic reaction, an infection, or tiny growths.

In an affected cavity a lining made of the same mucous membrane that is found in the nose becomes swollen and often blocks fluid drainage through the nasal passages.

Depending on which sinus is involved, the symptoms may include a headache, nasal congestion, sneezing, coughing, a discharge of pus from the nose, an apparent toothache, or fever. Untreated, the condition called sinusitis is likely to become chronic or, if infection is present, endanger the brain.

While no one can ascribe a positive function to the four types of head sinuses (frontal, ethmoidal, maxillary, and sphenoidal), some facts about them offer hints.

"We do know that in the classic sense sinuses really occur only in mammals and typically in those that have evolved large heads," said Dr. Jenkins, who is also Curator of Vertebrate Paleontology in the Harvard Museum of Comparative Zoology.

He pointed out, for example, that 50 to 55 million years ago during the Eocene epoch, characterized by the rise of mammals, the first horses were terrier sized and had either no sinuses or very small ones. As horses developed into larger animals what sinuses they had also grew so that today they are of considerable size.

The skull of an elephant has undergone extraordinary sinus development. Its frontal sinus extends far back in the head.

From these examples, one can conclude that sinuses are simply spaces that need not be filled with tissue or bone and therefore contribute to a lightening of what otherwise would be a heavy head.

Specialists in anatomy have also considered the possibility that sinuses

(Continued on Page 4)

Upper jaw sinus pain is often mistaken for a toothache.

When authorities in Massachusetts arrest a motorist on a charge of driving under the influence of alcohol, a finding of guilt or innocence often hinges on the outcome of a breath test.

An accused driver blows into a device containing a chemical solution. Any alcohol in his blood causes the solution's color to change from a dark yellow to a lighter tone. The degree of change determines the percentage of alcohol in the blood.

If the amount is .10 percent or more, the result would be sufficient to establish guilt. A motorist's refusal to take the test brings an automatic 90-day suspension of his license.

Captain James Port, Commander of the Traffic Section of the Massachusetts State Police, said that prior to obtaining breath analysis equipment in 1968 his department found it very difficult to secure a conviction for driving under the influence.

"The defense attorney would demand scientific proof of drunkenness, and we had little to offer," the captain declared. "With the availability of a breath analysis, we gained the tool we needed to prosecute successfully."

As breath testing contributes toward better law enforcement, the concept is also making inroads in health care.

On September 1, the MGH opened a Breath Analysis Laboratory in the hospital's new Ambulatory Care Center to diagnose certain gastrointestinal (GI) illnesses that beset both children and adults.

Directed by an MGH biochemist, Dr. Edward A. Carter, the laboratory evaluates the effect of various sugars on the gastrointestinal tract.

Unlike the police check for blood

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
J. Robert Buchanan, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIAL: *First of a series*

Under a Banner of Cost Containment

The movement toward making hospitals different but not necessarily better places has begun. Under a banner of cost containment, Massachusetts is trying to fiscally squeeze hospitals. Like college education, fuel, and food, hospital bills are indeed expensive. It might be instructive first to review how they began to soar.

In 1946 the federal Hill-Burton Act encouraged hospitals to expand. If there was a watershed event, though, it came on July 1, 1966, when Congress's Medicare and Medicaid bills became laws. Hospitals generally feared the impact. But the purpose was difficult to argue with: to entitle the elderly and the poor to first-class medical care. To a significant degree the two laws achieved their basic aims. At the same time they created a demand for equality of technology as well as equality of service. In the public mind this meant the local hospital needed the latest equipment regardless of whether 1 or 1,001 patients would benefit. If Massachusetts General Hospital acquired the second CT scan in North America, well it was time for Petaluma General Hospital to order one. That mentality manifested itself six months ago when the administrator of a tiny hospital in the Midwest called the MGH News Director to inquire whether Nuclear Magnetic Resonance (NMR) was ready for his hospital. A research tool of great promise, NMR needs much exploration to determine how best to deploy the device (*MGH News,* September 1982).

Complicated instruments like CT scans and one type of NMR cost roughly $1½ million to buy and tens of thousands of annual dollars to operate. The demand that Medicare–Medicaid created for technology also exploded into a public expectation of expensive new services. When fuel prices soared above the rest of the economy, they inflated the many hospital supplies dependent on oil in the manufacturing process. Employee salaries which had lagged behind the economy in the mid 1960s floated toward their rightful level. Since salaries account for about two of every three dollars spent by hospitals, the effect on costs was dramatic.

In 1974 the charge for a semiprivate room at the MGH was $118. By 1982 the figure had reached $255, and five other Boston hospitals charged more. Most businesses were experiencing the effects in the form of costly health care insurance provided as fringe benefits for employees. There is no wonder that business leaders were pressuring legislators to do something. No matter that technology has improved remarkably the quality of health care. Cost is the thing, and many perceive hospital costs as clearly too high.

Tests of the Breath Center on the Use Of Various Sugars

(Continued from Page 1)

alcohol, the MGH laboratory uses a device known as a gas chromatograph to determine whether a breath sample contains hydrogen gas and, if so, where it might be originating.

"The presence of hydrogen gas indicates that the patient's food is not being utilized properly," Dr. Carter said. "After the gas is produced, it circulates in the blood. Then upon reaching the lungs a certain amount of the gas filters out. We can subsequently capture it in the breath."

The sugars studied by the laboratory are lactose, so-called "milk sugar"; sucrose, which creates problems mainly in children; and lactulose, once employed extensively as a sweetener in cough medicines.

Seventy percent of the world's population, including 80 percent of all black people, cannot tolerate lactose in their diet.

High levels of lactose intolerance have been found in eastern Europe, the Orient, Mexico, South America, and Africa.

"For years well-meaning relief agencies have included powdered milk in food shipments to poverty-stricken people in Africa, only to wonder later why the recipients didn't seem healthier," Dr. Carter said.

"They continued to suffer episodes of abdominal pain, diarrhea, and flatulence [excessive gas in the digestive tract] because of lactose malabsorption."

If milk contained something that failed to agree with a person, the logical solution would be to avoid drinking milk. But the problem is more complex. Lactose turns up in many, many foods and also in drugs.

Dr. Carter recalled an elderly woman who had suffered a heart attack. Her cardiologist found it difficult to manage her condition because she experienced repeated attacks of diarrhea and flatulence.

Although the patient insisted that she had not consumed any milk products for years, a breath test showed an

Photographs: Page 8, courtesy of Mrs. Mildred Blood; all others by Myron Daniels.

Drawings: Page 4, MGH Medical Art Department; p. 7, courtesy of Dr. Allan H. Ropper.

John Murphy of Beacon Hill undergoes a lactulose intolerance test to check for possible bacterial overgrowth in his small intestine.

intolerance for lactose was having an effect on her.

It turned out that of six or seven medications prescribed for her heart condition several contained lactose as a binder or filler.

"The lactose in one or two of the drugs might not have bothered the patient," said Dr. Carter, "but taking a larger amount obviously had an adverse effect."

When a child suffers from diarrhea, loose stool, or abdominal cramps following meals and proves not to be lactose intolerant, the question of his or her ability to handle sucrose arises.

Much less common a problem than lactose, sucrose nevertheless can cause illness in people with certain genetic traits.

"And to eliminate sucrose from the diet is difficult," Dr. Carter added. "This sugar is even more common as a food sweetener than lactose."

To demonstrate bacterial overgrowth in the upper small intestine, the lactulose intolerance test is used.

The proliferation of bacteria in the small intestine, where they usually are not present, may interfere with normal small intestine function. In addition to chronic diarrhea, the patient may suffer considerable weight loss.

The physician may prescribe antibiotics to treat bacterial overgrowth.

Dr. Carter said that timing is important in testing for this condition. After the patient receives lactulose for purposes of the test, any intolerance in the small intestine would be reflected by early production of hydrogen gas.

On the gas chromatograph, a peak would appear within the first 30 minutes of the test, which involves taking a series of breath samples and processing them through the diagnostic instrument.

If the first peak does not occur until 90 minutes or so after start of the test, it means the sugar has reached the colon and that colonic bacteria are producing hydrogen, but as part of a usual normal role in the digestive process.

Timing for the sugar to go from "top-to-bottom" is carefully noted because in some patients the cause of diarrhea and flatulence is simply that the small intestine pushes the food through to the colon too rapidly.

This condition can sometimes be corrected with specific drugs.

In lectures that he presents on breath testing, Dr. Carter often mentions a 50-year-old woman physician who suffered from diabetes and chronic diarrhea, a situation not uncommon among diabetics. The diarrhea proved so uncontrollable that the doctor had to suspend her medical practice.

A lactulose breath test did not produce an early peak on the graph, indicating the small intestine was normal. Timing of the second peak showed that waste material was moving along at the correct rate.

Dr. Carter turned next to a lactose intolerance test.

"Under ordinary circumstances, it would also have been possible to determine any lactose intolerance by measuring blood glucose levels," he said. "But in this situation the glucose levels were already so abnormal because of the diabetes that they could not be properly interpreted as far as lactose was concerned."

It was fortunate the breath test could be conducted because the patient proved to be very lactose intolerant.

Physicians advised her to add to milk an ingredient that breaks down lactose and to avoid other foods containing the sugar. The physician-patient's health improved, and she was able to resume her medical interests.

Drs. Kurt J. Isselbacher, Chief of the MGH's GI Unit, and W. Allan Walker, head of the Pediatric GI Unit, jointly supervise the Breath Analysis Laboratory. One of a small but growing number of such facilities at medical centers around the nation, the laboratory performs a welcome service in assessing the nutritional status of patients.

"Knowing how well a person's body utilizes food is crucial," Dr. Carter said, "for the proper growth of children . . . to meet the changing needs of people as they advance in age . . . and in treating sick or injured patients who often require special diets." ■

Technician Linda Jacobson feeds breath sample into gas chromatograph for processing.

Most Sinus Attacks Can Be Blamed On Allergies

(Continued from Page 1)

evolved to help protect the skull. By their unique design and strategic locations, they do provide a resiliency from impact.

Another feature of sinuses is their role as resonating chambers. The sinuses of primates are fashioned like those of man, and everyone knows how the roars of a large ape resound throughout a jungle.

How often have you heard that a singer had to postpone a performance because of a heavy cold? Often it is the effect of the cold on the sinuses that produced the minor crisis.

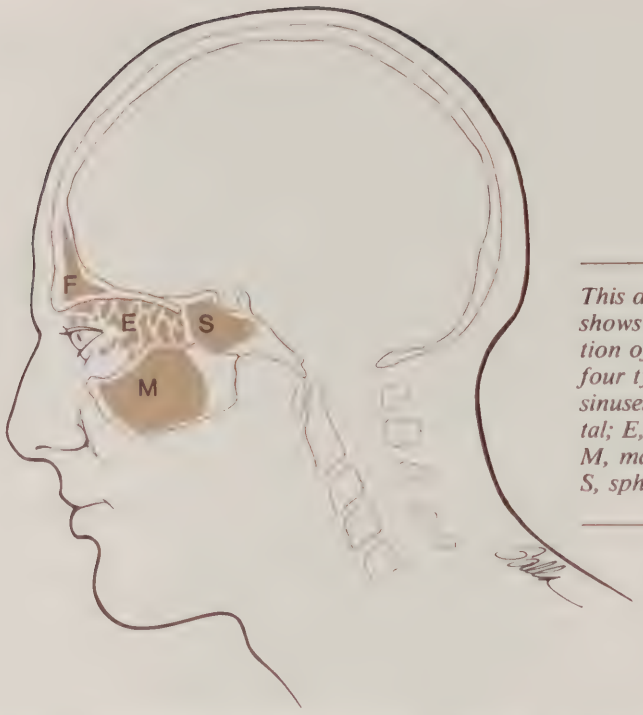
In the vast majority of sinusitis episodes, doctors attribute the cause to an allergy. The patient might have been hypersensitive to any one of an endless array of possibilities: dust, pollen, ragweed, animal hairs, feathers, insects, smoke, certain foods, etc. The chance of infection developing increases if fluids in the sinuses fail to drain.

When an infection itself is the direct cause of sinusitis, the examining physician labels an upper respiratory virus (often a common cold) as the most frequent culprit. But the cause may also be bacterial, such as streptococci, pneumococci, or Hemophilus influenzae (H flu). Polyps, tiny teardrop-shaped growths, represent a third possible cause.

Of the sinuses most commonly involved, the two frontal (over the eyebrows) and the two maxillary (behind the cheeks) lead the list. The patient with frontal sinusitis often finds his facial pain intensified as he bends forward or taps the affected area. As for the maxillary patient, he frequently mistakes his sinus pain for a toothache.

Patients stricken in a third type of sinus, the sponge-like ethmoid (situated on each side of the upper nose), complain of pain in the nose, behind the eyes, or at the sides of the head, particularly back of the ears.

Dr. Ann S. Baker, a physician in the MGH Infectious Disease Unit, described the ethmoid sinus as the chief problem site for children with sinusitis. This is because the ethmoid spaces develop in children at a young age, she said, while full development of the frontal, maxillary, and sphenoidal is not achieved until adolescence.



This drawing shows the location of the head's four types of sinuses: F, frontal; E, ethmoid; M, maxillary; and S, sphenoid.

Because the single sphenoidal sinus lies deep within the cranium behind the upper part of the nose, physicians can on initial evaluation easily misdiagnose infection in that cavity as some other neurologic disorder, thus delaying appropriate treatment.

To provide greater insights into infectious sphenoidal sinusitis, an MGH–Massachusetts Eye and Ear Infirmary (M.E.E.I.) medical team has reviewed data between 1968 and 1980 on 30 patients treated for the condition at the two hospitals.

The team consisted of Drs. Baker, Daniel Lew, and Frederick S. Southwick of the MGH and, from the neighboring M.E.E.I., Drs. William W. Montgomery and Alfred L. Weber.

In a report to a meeting of infectious disease specialists in Miami last month, the team said that in the acute disease early diagnosis and aggressive treatment including surgical drainage proved critical. Delays in treatment were always associated with serious setbacks or death.

Fortunately, during the 12-year study period in the two institutions, infectious sphenoidal sinusitis represented less than 3 percent of the 1,087 patients observed with various forms of sinus disease.

The patient with sphenoidal sinusitis may complain of pain in any part of the head but frequently feels the most severe aching at the vertex, or top, of the head.

Regardless of which sinus becomes inflamed or the cause, restoration of drainage leads in priority of treatment, said Dr. Baker, who is also Consultant in Infectious Diseases at the M.E.E.I. and Assistant Professor of Medicine at Harvard Medical School.

She said medications containing antihistamines or epinephrine can shrink the nasal membranes in the allergic patient. She recommends use of a nasal spray and then several minutes of breathing through a hot towel. Hot showers also help.

Presence of an infection calls for antibiotic therapy. Dr. Baker said penicillin, ampicillin, and erythromycin are effective. If X rays taken two weeks after the start of antibiotics fail to show complete resolution of the infection, the drugs should be continued for another two weeks.

Repeated episodes of infection with a thickening of the mucous membrane and continual partial drainage obstructions may lead to chronic sinusitis and a need for surgery.

When pain and/or infection persists in a chronic frontal sinus, the cavity may be exposed surgically, cleaned out, filled with fatty tissue from the abdomen, and then sealed.

Dr. Montgomery, a senior surgeon at the M.E.E.I. and Professor of Otolaryngology at Harvard Medical School, devised this operation, called an osteoplastic frontal obliteration, and pioneered its use in the United States.

He said the operation "provides an almost sure cure for chronic frontal sinusitis whereas fewer than half of such patients were cured earlier."

A major risk in frontal sinusitis is that the cavity's membranous lining may form a cyst (a sac containing liquid or semisolid material). Gradually expanding, the cyst could distend

the sinus walls.

Often upon surgery doctors find the posterior wall destroyed and only a cyst wall standing between the sinus and the brain's outermost protective membrane, the dura. Should the cyst break, life-threatening infection could result.

Polyp disease frequently accounts for ethmoid surgery. "Picture the sinus as a velvet-lined cup turned upside down," suggested Dr. William Wilson, another M.E.E.I. surgeon and Harvard professor, in describing the problem. "The velvet becomes so thick it not only fills the cup but also begins to hang down into the nose.

"A surgeon in an office could snare out a few polyps, but if a lot of polyps are present, obstructing the flow of mucus and allowing bacteria to proliferate, surgery is needed."

In conducting ethmoid surgery, the doctor can work through a nostril or make an exterior incision at about the point on the side of the nose where eye glasses normally rest. To reach a sphenoidal sinus, a surgeon usually penetrates the ethmoid first.

Many polyps may reside in the walnut-sized maxillary sinus but cause no problems. Surgery becomes necessary when either antibiotics fail to dispose of an infection or, because of a very swollen sinus, a polyp extrudes into the nose.

This repair work is called the Caldwell-Luc operation, honoring two turn-of-the-century physicians. The procedure involves entering the sinus through the inside of the mouth, removing contents of the sinus, and then constructing a new and larger opening for drainage through the nose.

No one really knows how many people experience sinus discomfort, but Dr. Montgomery remarked, "Every time a person catches a cold, he gets some degree of sinusitis."

For most people a home or drugstore remedy provides adequate relief. The more complicated conditions need professional help.

To avoid provoking a sinusitis attack, patients are advised by doctors not to swim under water or engage in scuba diving. For patients who must travel by air or visit a high altitude region, an oral decongestant and a nasal spray are suggested as a precautionary measure.

Dr. Montgomery sees no validity to the popular belief that if a sinusitis patient moves from a chilly, damp region to a warm, dry area, such as in America's Southwest, the condition will improve.

"By inducing such patients to move, for example, to the Southwest," he said, "all the myth has done is increase the incidence of sinusitis in that part of the country." ■

A Germ Fighter With a Dual Personality

As with any army on the move, the human body's germ-fighting network — the so-called immune system — relies on an interaction of brains and brawn.

Each day protective white blood cells course over a total of 60,000 miles of veins and arteries, ever on guard against a possible invasion of disease-causing organisms.

Although they pick off their own share of agents that produce infection, lymphocytes are essentially tacticians. They point the way for muscle men called phagocytes, comprised of neutrophils and monocytes, to move against germs and literally gobble them up.

The process known as phagocytosis works like this: When bacteria, for example, penetrate the body, lymphocytes produce defenders called antibodies. These combine with a complex series of proteins which recognize bacteria. The result is a substance called opsonin, meaning relish in Latin. Opsonin coats the bacteria, in effect drawing the phagocytes to their prey.

The phenomenon of serum opsonizing bacteria was discovered around the turn of the century and drew such public attention that George Bernard Shaw dwelled at length on phagocytosis in his play, *The Doctor's Dilemma.* At one point, he wrote, "The microbes are nicely buttered for the phagocytes."

Sometimes, however, the defensive strategy goes awry. Studies conducted in the MGH Hematology-Oncology Unit, directed by Dr. Thomas P. Stossel, indicate that a very delicate balance exists between the protective effect of phagocytes and a reaction harmful to health.

To kill bacteria, phagocytes combine with oxygen to form very toxic chemical compounds called oxygen metabolites. Normally, healthy parts of the body have the means to protect themselves from this toxicity, but MGH researchers have found that under certain circumstances the oxygen metabolites can cause any one of a number of disorders.

The injurious response could be severe dental disease, genetic damage, inflammatory conditions of various kinds, such as those involved in arthritis, or, it is suspected, even cancer.

Dr. Stossel's team first demonstrated that phagocytes could produce mutations in bacteria. Then the researchers showed that the usually protective cells could also damage mammalian cells.

Of particular importance was a find-

(Concluded on Page 6)

Dr. Sigmund Weitzman (right) conferring with Dr. Thomas Stossel on a phagocyte study

Possible Way to Avoid Cell's Harm

(Concluded from Page 5)

ing of genetic damage. Dr. Stossel described the genetic harm as shotgun-like, rather than specific, but said, "if enough genetic material were damaged, the making of new cells in a tissue would stop, and the tissue would degenerate."

The MGH work has raised a suspicion that the nonspecific genetic damage may be a key step leading to cancer.

"Much of our research is focused on trying to prove whether or not this is so," said Dr. Stossel, who earlier this year at the age of 40 was promoted to Professor of Medicine at Harvard Medical School.

Recently in the *Journal of Immunology* the MGH specialist and a unit colleague, Dr. Sigmund Weitzman, reported that certain chemicals have an ability to block the harmful action of phagocytes by sopping up the oxygen metabolites. He stressed, however, that these studies are still in the beginning stage. Successful in bacteria, the chemicals have yet to prove their protective powers in mammalian cells.

Phagocytes are born in the bone marrow, which produces 100 billion neutrophils daily. This can increase tenfold in the face of disease.

Dr. Stossel likened the neutrophils to "crawlers" because they go on the attack when foreign organisms invade. He termed monocytes "sentries" because they develop into another type of cell, a macrophage, and guard filter organs such as the spleen, liver, lungs, and lymph nodes. Germs slipping by the neutrophils are picked off by the sentries.

Once known as the reticuloendothelial system, the guard network is now referred to simply as the macrophage system.

Because phagocytes are not always finely tuned enough to protect against infection, problems do arise.

Dr. Stossel told of treating patients whose bone marrow either stopped making phagocytes or began producing faulty white cells that just failed to do their job.

At times when a spreading (metastasizing) cancer affects the bone marrow, the output of both neutrophils and monocytes ceases, thus leaving the patient highly susceptible to infection.

Sometimes lymphocytes fail to make the antibodies they are supposed to. If this happens, phagocytosis cannot proceed.

Drug treatment (chemotherapy) for cancer has a toxic effect on both sick cells and healthy ones, with phagocytes among the normal ones most susceptible to the toxicity.

The idea behind chemotherapy is that upon exposure to the drugs cancerous cells will die quicker than normal ones. Once the sick cells vanish, the chemotherapy can be stopped, and surviving noncancerous cells can regain their health.

Loss of a spleen can also weaken phagocytic action. This organ does an excellent job of snaring bacteria and therefore attracts a heavy population of macrophages. But the spleen can fall victim to many maladies.

Speaking recently to a gathering of colleagues at an MGH Grand Rounds, Dr. Stossel outlined some of the dilemmas that phagocyte disorders can pose.

In addition to genetic damage and the possibility of cancer, he discussed a severe dental disease called juvenile periodontosis and exhibited a slide showing a boy whose jawbone had greatly deteriorated. The disease had released a toxin which prevented phagocytes from entering the boy's mouth tissue to control the organisms.

It has long been known, the doctor said, that people with aplastic anemia and leukemia have trouble with oral hygiene, possibly due to some foreign toxin.

And Dr. Stossel spoke of very sick people with a general inflammation that causes severe, sometimes fatal, lung damage. Working with a team of anesthesia specialists headed by Dr. Warren M. Zapol, Dr. Stossel and his investigators, including Drs. Stuart Lind and David Smith, hope to learn what role phagocytes might play in this illness, known as acute respiratory distress syndrome.

"There is evidence that phagocytes become stuck in the lungs and damage them with the same agents they use to kill bacteria," explained Dr. Stossel, who is also Editor-in-Chief of the *Journal of Clinical Investigation*, a prestigious medical publication based at the MGH.

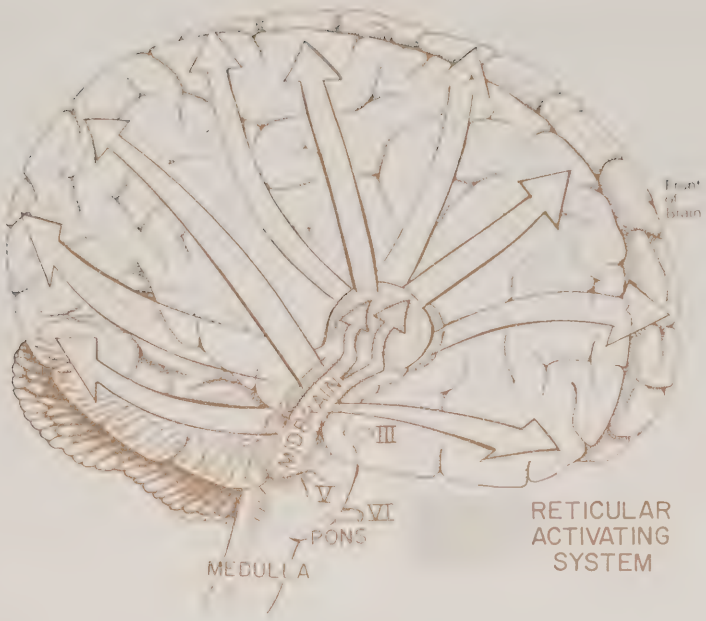
In addition to collaborating with the hospital's Anesthesia Department, the Hematology–Oncology Unit works closely with the MGH Renal, Infectious Disease, and Developmental Biology Units.

Research funding comes from a variety of sources, including in part the National Institutes of Health, Muscular Dystrophy Association, American Heart Association, American Cancer Society, Edwin S. Webster Foundation, Arthur O. and Gullan M. Wellman, and Edwin W. Hiam.

"It is clear that phagocytes are like a double-edged sword," said Dr. Stossel. "They perform an invaluable service in protecting health, but they are simultaneously vulnerable to the vagaries of nature and may inflict harm.

"Hopefully, at some point down the road, we will be able to engineer an appropriate response when these inherently good cells go astray." ■

Using an inverted, light microscope, Dr. John Hartwig magnifies a macrophage specimen 2,000 times to view the cell's action on a television screen.



Damage to the midbrain's Reticular Activating System could halt signals to all parts of the brain, thereby causing coma.

Focusing Some Light on Coma

Feeling exhausted while driving home from what had been a very lively Christmas party, Tim Blood pulled his car off the road and slumped behind the wheel to doze.

"I remember dreaming of lush, green fields in Vermont with a stream coursing through the pasture land and with mountains in the background," he said. "I had always wanted to own a chalet, and in my dream I saw one that I pictured as mine. The setting was so peaceful I didn't want to leave."

When the 17-year-old youth awoke, he was no longer in his car but in the Neurological–Neurosurgical Intensive Care Unit of the MGH. And the time was not several hours later. Ten days had elapsed!

The Southboro, Mass., high school senior had forgotten to turn off the car's engine, and as he slept carbon monoxide seeped into the vehicle. The fumes reduced the levels of oxygen in the young man's blood, in effect putting his brain cells to sleep.

Many other victims of a coma as deep as Tim's have either failed to survive or recovered with some persistent impairment. Tim was fortunate. He enjoyed a full, albeit gradual, return to good health.

Taken first to Marlboro Hospital, the comatose patient was transferred after only one day to the MGH for more specialized attention. Besides the coma, his brain had begun to swell.

With a device (subdural bolt) installed in the skull to measure pressure within the head (*MGH News,* April 1981), MGH specialists were able to use drugs to control and ultimately overcome the swelling.

When the effects of the carbon monoxide wore off and Tim came to, he required another week in the intensive care unit and then four weeks in the hospital's Rehabilitation Unit.

"At first I couldn't recognize my parents or my girl friend," he said as he reflected on the events of nearly three years ago. "And I had trouble writing and walking."

For some time after the near tragedy, memory lapses forced Tim to carry a notebook in which to jot down reminders. But today his mind is once more keen. He has worked as a computer operator since shortly after his high school graduation in 1980.

What actually is coma which each year strikes so many Americans like Tim?

Dr. Allan H. Ropper, who codirects the MGH Neurological–Neurosurgical ICU, described coma as total unresponsiveness to the environment, even when the patient is stimulated.

"One may move his eyes or limbs and still be unconscious," he said, "but if the patient performs these actions in a purposeful way, then he is not in a coma."

It is possible to appear completely unresponsive, yet have a normal consciousness. The condition, called the "locked-in" syndrome, sometimes develops when a stroke (usually the result of blockage of a blood vessel) occurs in the brain stem.

"What happens," said Dr. Ropper, "is that all of the passages for brain signals to reach the face, the vocal cords, the limbs, and so forth, are damaged. So that the patient's brain may function well and he can see and understand what is happening around him, but he cannot respond."

While a number of situations such as a head injury, disease, drug abuse, or ingestion of poison can set the stage for coma, one of two developments must take place within the brain itself before coma can actually come about.

To become comatose, a person must have suffered damage either to the midbrain's thumbnail size portion known as the Reticular Activating System (RAS) or to *both* halves, or hemispheres, of the brain's largest and most important area, the cerebrum. This region accounts in the main for man's intelligence.

To carry out their natural functions related to seeing, hearing, talking, calculating, memorizing, etc., the hemispheres rely upon impulses from the RAS.

Damage to the RAS could come from blockage of a blood vessel in the midbrain; compression of the area, possibly by a tumor or large hemorrhage; or direct bruising because of a head injury.

Dr. Ropper described such bruising as uncommon. Of a group of 250 patients who suffered head injuries during the past five years, he found only three individuals whose coma could be attributed to RAS bruising.

"Damage to both hemispheres is by far the most common cause of coma," said the doctor, who is also Assistant

(Concluded on Page 8)

Semiconscious?

Laymen commonly refer to a partially conscious person as being semiconscious.

Physicians, however, try to avoid this expression.

"The word semicoma is really too vague to have any useful medical meaning," said Dr. Allan Ropper of the Neurology Service.

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street
Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Reversing Coma Depends on Its Cause

(Concluded from Page 7)

Professor of Neurology at Harvard Medical School. "If both halves are harmed, it doesn't really matter whether the Reticular Activating System is working or not. The messages can't get through."

Overdoses of drugs cause comas by halting nerve cell function in both hemispheres. Blood clots atop the brain (subdural hematomas), often the result of blows to the head, may generate coma by compressing both sides of the brain.

Unless it affects the RAS, a stroke generally does not lead to unconsciousness. Most strokes injure a portion of one side of the brain or the other, but not both.

Low blood flow to the entire brain, possibly due to a sudden heart stoppage (cardiac arrest), frequently presents a serious comatose situation.

After coma has set in, the brain's RAS may give the patient an appearance of alertness, even opening his eyes; yet, because of widespread damage to both cerebral cortexes, the coverings of the hemispheres, the patient has no consciousness and is in what physicians term a vegetative state.

Reversing a coma depends on what produced it. Affected by drugs alone, a coma will terminate when their influence wanes and the brain cells reactivate.

"It's much like the action of Novocain in deadening a nerve so that a dentist can pull a tooth, fill a deep cavity, or treat the gum," Dr. Ropper said. "As soon as the Novocain wears off, the patient regains full sensitivity in the treated area."

Sometimes in triggering coma, a drug will also attack the brain's respiratory centers and stop a patient's breathing. As his blood oxygen levels fall, his heart becomes impaired. In treating such a patient, physicians would first seek resumption of adequate airway ventilation, then move to restore proper blood pressure.

While no one can say with certainty when a comatose person will awaken, specific combinations of neurological signs during the early phase of a coma appear to be highly predictive of a good or bad outcome.

If over a 24-hour period, for example, examination of a comatose patient fails to detect any eye movement, pupillary reaction, or purposeful motor activity, chances of the individual dying or becoming vegetative range as high as 98 percent.

Dr. Ropper said that awakenings from drug overdoses may average more than 90 percent in a hospital treating a large number of such conditions. Of patients comatose from head injuries, 60 percent may reawaken. Comas due to other conditions such as cardiac arrest or lack of oxygen (anoxia) have anywhere from a 60 to 90 percent chance of ending.

Emerging from a metabolic coma (resulting from a chemical produced by a damaged organ, such as failure of the kidney or liver) really depends on effective treatment of the underlying condition. A patient unconscious from encephalitis will awaken when the virus goes away. More thyroid hormone can be the solution for a coma created by a low thyroid problem (myxedema).

After 10 days in a coma from carbon monoxide fumes, Timothy Blood made a complete recovery.

In general the longer a person remains unconscious, the less likely he is to awaken, especially if the coma results from structural damage to the brain.

Children are often an exception. "They can be unconscious for as long as a year and still recover," Dr. Ropper declared. "Perhaps some fundamental feature of a developing brain enables it to withstand injuries.

"However, I don't know of any adult unresponsive for longer than four or six months who has had a meaningful recovery. Occasionally vegetative individuals regain some intellectual function."

In an effort to learn more about coma, physicians in the MGH Neurological-Neurosurgical ICU employ a special EEG (electroencephalograph) to monitor brain wave changes in comatose patients.

The changes can be very subtle, coming in little blocks, like sleep and wake cycles. But they may clearly show greater activity in one patient than in another. Specialists think an ability to produce such blocks or cycles may well indicate that RAS messages are getting through again.

Faced with the uncertainties that coma presents, relatives and friends of an unconscious person should be realistic.

"Be patient and hope for improvement," Dr. Ropper advised, "but as time passes without change in the patient's condition, try to accept the idea that he may remain severely impaired.

"Recognize that in all likelihood the patient is not aware of his plight, thus is not suffering.

"And if and when the patient emerges from his coma, be ready to supply lots of encouragement, which is so important in facilitating a recovery." ■

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 41 No. 9 December, 1982

Trying to Solve a Medical Enigma: Mass Hysteria

MGH Aids Development of Ill Newborns

A dozen years ago tiny, premature babies fought almost insurmountable odds to stay alive.

Often plagued by a lung, heart, or neurological problem, or a combination of illnesses, most of the infants died. Of every 10 newborns weighing under 2¼ pounds (1,000 grams), nine succumbed.

Since then, improvements in neonatal intensive care have turned the tide.

Today, with diagnostic techniques such as the computed tomography (CT) scan and ultrasound and with other high technology equipment, like breathing control devices, newborn intensive care units (ICUs) save most preemies.

The chances of survival for premature babies weighing less than 3¼ pounds (about 1,500 grams) but more than 1⅔ pounds (750 grams) are currently greater than 60 percent. Most survivors are normal; major neuro-developmental disabilities occur in only about 14 percent of this population. That figure compares with a greater than 50 percent incidence in the pre-ICU era.

"At the MGH," according to Dr. Kalpathy S. Krishnamoorthy, a specialist in pediatric neurology, "almost 65 percent of our Newborn ICU graduates are doing really well, and 25 percent have shown only minor neuro-developmental problems."

A study conducted by Dr. Daniel C. Shannon, MGH Chief of Pediatric Pulmonary Research and former head of the Pediatric and Newborn ICUs, showed that the cost of ICU care for MGH infants is less per patient than the cost of treating a critically ill adult. Also, the study indicated a *(Continued on Page 4)*

Treated two weeks after birth for a serious brain disorder, Allison Hooper, shown at right in photo at two years of age, is clearly as healthy as her normal twin, Brook.

Near the close of the Middle Ages entire towns in Germany, France, and Italy were caught up in waves of frenzy.

Calling out the names of evil spirits, men and women ran from their homes and danced in the streets until they collapsed from exhaustion.

For two centuries accounts of these dancing manias appeared sporadically in the medical literature but never accompanied by an explanation for this mass hysteria.

Even in modern times similar events have taken place in parts of Africa. Hundreds of tribesmen scurried through villages in Uganda in 1964 "on instructions from the spirits of leaders long gone." The hysteria lasted a month. In neighboring Tanzania, a display of another kind occurred. Lasting many months, it was marked by uncontrollable laughter.

In this country, many still recall Orson Welles' War of the Worlds radio broadcast in 1938. Although announcers repeated over and over that the account of a Martian invasion was fictional, many Americans panicked. Of more than six million people who heard the program, approximately one-fourth thought the event being dramatized was real.

In the late 1950s in Seattle, then under a cloud of concern about hydrogen bomb testing, people began to notice black particles on their cars. Rumors that the particles were from radioactive fallout touched off a panic. It ended only after officials convinced the public that the dust stemmed from improper combustion of coal in the environment. What's more, the dust had been gathering on cars for years.

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206
Martin S. Bander, *Editor*
Myron H. Daniels, *Assistant Editor*
Doris G. Schreckengaust, *Copyreader*

EDITORIAL BOARD
J. Robert Buchanan, MD, *General Director*
Kurt J. Isselbacher, MD, *Research, Medicine*
Paul S. Russell, MD, *Surgery*
Ronald A. Malt, MD, *Surgery*
Roger H. Sweet, MD, *Utilization*
Stanley Bennett, *Photography*
Robert J. Galla, *Typography*

EDITORIAL:

Why Boston Hospitals Are So Expensive

Newspapers have made much lately of the fact that the average stay in a Boston hospital costs more than in any other American city. Putting that statement in perspective might prove enlightening. First of all, the major teaching hospitals in New York City charge much more per room each day than their Boston counterparts. Boston may or may not be the most expensive American city in which to be hospitalized. Regardless, why then does a stay in a Boston hospital cost so much? For one thing teaching hospitals by their nature provide the most advanced care, and that inevitably costs more. Combine this information with the fact that Boston almost certainly has a higher ratio of teaching hospitals to community hospitals than any other city in the country. For that reason alone Boston hospitals as a group *should* have higher costs than those of other cities.

A concomitant of Boston's cluster of teaching hospitals is the large number of very sick patients referred to them, many from out of state. These patients tend to have difficult-to-diagnose, difficult-to-treat problems. In fact they often have several major illnesses. As a consequence they remain hospitalized longer, and their total bill is naturally higher.

An aging population compounds the difficulty. Massachusetts has about 1.4 percent more over-65 populace than the national average. For the over-75 group Massachusetts has .9 percent more than the national average. It is obvious that the elderly use health care beds at a much higher rate than their younger countrymen. The over-75 patients use eight times as many hospital days as those under 65. That is why even small percentage differences in elderly translate to major increased per capita costs.

Under the federal Medicaid law, each state sets its own benefit limits. In contrast to many states, Massachusetts has provided every coverage the law allows. Maximizing benefits also maximizes costs. When one examines the underlying reasons then, there should be no surprise that Boston charges for total stay – not for room rates – lead the nation. Besides higher costs, Boston teaching hospitals offer benefits that attract patients from around the world. They come in spite of the costs. What attracts them? Next in this series we will consider some of the things Boston teaching hospitals must be doing right.

Losses in Childhood May Help Explain Some Hysteria

(Continued from Page 1)

A compilation of reports of epidemic hysteria occurring at home and abroad between 1900 and 1979 shows that of 37 incidents 23, or 62 percent, happened at schools.

One school outbreak in the Boston suburb of Norwood in which 34 of 224 students were hospitalized intrigued two MGH psychiatrists, Drs. Gary W. Small and Armand M. Nicholi, Jr.

They searched for some clue as to what might have contributed to the incident. Their findings appeared in the June 1982 issue of a scientific journal, Archives of General Psychiatry.

Dr. Small, now with the UCLA School of Medicine in Los Angeles, and Dr. Nicholi wrote: "A significantly higher rate of parental divorce and death within the family occurred among the hospitalized children. These findings suggest a relationship between childhood loss and susceptibility to mass hysteria."

The hysteria erupted in the auditorium of an elementary school as the 224 students were watching or participating in a rehearsal of a play staged by sixth graders to celebrate their graduation. A sixth-grade boy, a class leader, suddenly became dizzy and fell from the stage, cutting his chin.

As teachers assisted the boy who was bleeding profusely, other children began to feel weak, dizzy, faint, and nauseated, and to experience chills and abdominal pain.

Bewildered school officials, fearing some environmental contaminant, alerted the fire department which ordered evacuation of the building.

Unfounded rumors as to the cause of the incident, such as toxic fumes, gas leaks, food poisoning, and the like, made additional youngsters feel sick. Sirens of approaching emergency vehicles heightened the chaos.

As the more severely ill were taken to a hospital, a team of physicians and nurses cared for the less affected children on the school lawn.

Symptoms began to subside as medi-

Photographs: Page 1, MGH Photo Lab; all others, Myron Daniels

Drawings: Page 3, MGH Archives; pp. 5 (upper), 6, 7 (lower), courtesy of Arnold Arboretum

At a hospital in 19th century Paris, famed neurologist Jean M. Charcot demonstrates to colleagues how he treats a patient suffering from hysteria.

cal personnel assured both children and parents that the illness was nothing to worry about. Four hours after the outbreak started, it was over.

In their study, Drs. Small and Nicholi found that the epidemic in Norwood, a predominantly upper-middle-class town of 30,000, contained characteristic features of mass hysteria that had been reported in other outbreaks:

- A preponderance of illness in girls
- Apparent transmission of illness by sight and/or sound
- Presence of hyperventilation (rapid and deep breathing)
- Absence of physical findings
- Evidence of unusual physical and/or psychological stress which took the form of anticipated loss.

Just a few days earlier, local newspapers had announced that the school's admired and respected principal was about to be transferred. Many parents signed a petition opposing his departure.

In the light of research by Dr. Nicholi and others which had suggested that current loss often reactivates memories of a serious loss earlier in life, Drs. Small and Nicholi obtained personal data from families of those in the school outbreak. Of the 224 students involved, responses came from families representing 182 (81 percent).

"The rate of parental divorce for the hospitalized children was 47 percent compared with 10 percent for those not hospitalized," the psychiatrists reported. "Death within the family occurred in 74 percent of the hospitalized group compared with 39 percent of the nonhospitalized group."

Most of the deaths involved occurred outside the immediate family.

In a recent interview, Dr. Small said that although much research has suggested the importance of the death of a parent during childhood as a contributing factor in psychological illness, the study he and Dr. Nicholi conducted underscored the importance of loss of members of the extended family as well.

Dr. Small also pointed out that the study findings pertain to just one epidemic where psychological stress took the form of impending loss. Many kinds of psychological stress, such as that arising from concern over environmental pollution, can contribute to mass hysteria, he said.

Dr. Nicholi said in an interview that he thinks children are more fearful of being abandoned through death or divorce than people realize.

"This fear of abandonment is the first fear we encounter in life," he said. "When a mother leaves a baby, the infant will often cry because it doesn't know when, or if, the mother plans to return.

"A death in the family reactivates the abandonment fear in a child, and seeing others cry in grief accentuates the effect upon him."

Some years ago, Dr. Nicholi studied a group of students who had dropped out of Harvard University for psychiatric reasons. He found that among those with the most severe illness (schizophrenia) a statistically significant higher percentage had lost a parent through death.

Those with less severe illnesses had the next highest incidence. A control group (established among nondropouts to afford a standard of comparison in the study) had the lowest exposure to parental death.

Dr. Nicholi said that as he explored this first hint of a possible relationship between loss of a parent and having an emotional disorder he realized the death of a parent was only one form of absence. He could be "missing" through divorce or even because of a time-consuming job.

Dr. Nicholi wrote a number of papers on this in collaboration with a Harvard University colleague, Dr. Norman Watt, now of the University of Colorado.

American parents spend less time today with their children than parents in perhaps every other nation in the world. One reason Dr. Nicholi said, is that in many families both the fathers and the mothers have to hold jobs to make ends meet.

In the past 15 years the divorce rate in the United States has soared. Starting at the same time as the divorce jump was a parallel trend in the illegal use of mind-altering drugs.

"This began with a small group of college students on the east and west coasts," said the MGH psychiatrist. "Today, millions across the nation, people of all ages and from all socio-economic groups, are caught up in the drug craze. Some 20 million people alone smoke marijuana daily."

Just as he sought to learn what lies behind certain forms of epidemic hysteria, Dr. Nicholi hopes to discover why some people crave drugs.

"One finds that although drug users differ significantly from much of the rest of the population," he said, "their traits of anger, depression, and low self-esteem are the same as those found so often in families where parents are absent or inaccessible."

Dr. Nicholi believes there are reasons for optimism, however, on two fronts:

"We're beginning to see a gradual change in life-styles in our country. During the past 6 months, for the first time in 15 years, there has been a leveling off in both the divorce rate and the illegal use of drugs." ■

Dr. Joseph Custer, Associate Director of the Pediatric and Newborn Intensive Care Units, instructs staff nurses in patient management.

Brighter Future for Intensive Care Infants

(Continued from Page 1)

more acceptable level of function among the infant survivors than among their adult counterparts.

But what of the future of these children? After modern intensive care enables many babies to overcome an immediate crisis, how do these children fare as months and years go by?

Without a doubt much better than premature infants of a few decades ago, said Dr. Krishnamoorthy and Kristen J. Kuehnle, Ed.D., a psychologist.

Together they maintain a close check on the growth and development of hundreds of children who have undergone critical care in the MGH's Newborn ICU. Although the MGH does not deliver babies, the unit treats newborns who are critically ill and transferred here soon after birth.

As Dr. Krishnamoorthy oversees careful assessment of each child's physical progress, with special attention paid to neurological status, Dr. Kuehnle conducts testing to assess for any subtle learning and/or psychological problems that may exist.

They said that although the majority of the children do well a small portion may have hearing, language, or motor problems, attention deficits, or perceptual difficulties.

"Some people assert that a child would outgrow these immaturities," Dr. Kuehnle said, "but our experience has shown that such is not necessarily the case. However, if these conditions are detected early, they can often be dealt with effectively before the child enters school."

Many youngsters with lagging motor skills turn out to have overprotective parents. Unknowingly they look upon their low birth weight children as fragile and therefore impose restrictions on activities normal for others of the same age. "In effect what the parents are doing," Dr. Kuehnle said, "is holding back their child's development."

Parents can and do misinterpret other of their child's behavior. "Why can't he sit still? Why is he so destructive?" they may ask.

Dr. Kalpathy Krishnamoorthy checks on infant in Newborn ICU.

"This is where we sometimes find perceptual or attentional deficits," Dr. Kuehnle declared. "By advising the parents of the real problem and how to handle it, we can end their tendency to regard the children as difficult." (*MGH News,* December 1981)

Low birth weight does not in itself threaten intellectual impairment. In general, children born prematurely have intelligence levels ranging from low average to superior. One baby treated in the MGH Newborn ICU was found later to have an IQ of 134 (very superior).

A serious risk that often does accompany premature birth, however, is the threat of bleeding in the brain (intracranial hemorrhage). This was a major impetus for starting the Newborn Intensive Care Follow-up Program, directed by Dr. Krishnamoorthy.

Initially among the babies seen in the Newborn ICU, two-thirds were suffering from respiratory distress syndrome (hyaline membrane disease) which caused the lungs to collapse with each breath. Another 15 percent or so had a heart condition, and most of the remainder were afflicted with a neurological illness (*MGH News,* May 1973).

Autopsies on premature infants who failed to survive led to an important discovery. "Even though most of the children had undergone treatment for a lung or heart problem," Dr. Krishnamoorthy said, "the autopsies revealed brain hemorrhages in 60 to 80 percent of the infants. The bleeding was not detected until after death."

During the 1970s, availability of the CT scan and ultrasound not only made it possible to spot the hemorrhaging but also to show that the patient could often survive despite the bleeding.

"By closely controlling levels of oxygen, sugar, acidity, and bile pigments in the blood, as well as blood pressure, we found that a hemorrhage, if small, would often stop on its own," said the MGH pediatric neurologist.

(Dr. Krishnamoorthy was principal author of a scientific paper on survivors of neonatal brain hemorrhages which was read at a Perinatal Intracranial Hemorrhage Conference in Washington, D.C.)

But, again, what of the future? Were the children being saved only to become high risks later for such conditions as cerebral palsy or hydrocephalus (excessive spinal fluid in the brain causing pressure on surrounding tissues)?

Prior to the opening of newborn ICUs, a high percentage of premature

Making the Holidays Safer for Children

Family gatherings . . . friends and neighbors dropping by . . . the kitchen a scene of hustle and bustle . . . little ones fending for themselves.

Christmas is a busy time of the year when celebrating the holiday displaces normal household routines.

Around the home colorful plants and decorations invite attention while a gaily bedecked tree glitters in a corner of the living room.

Christmas touches in a home can have a hypnotic effect upon little children. Coupled with the distractions that naturally befall a host and hostess, the scene can pose serious hazards for the more curious tot.

Children aged two and under have an affinity for popping objects into their mouth. An older youngster may satisfy his curiosity by touching, twisting, or squeezing.

Placed out of the reach of children, plants are harmless. When eaten, bruised, or crushed, however, certain plants, including many popular at Christmas, may provoke bodily reac-

(Continued on Page 6)

Keep little children away from tempting holly berries.

infants developed cerebral palsy as a result of some birth-related insult to their brain. Over the years since then, the percentage of stricken babies has plummeted, but the danger has not vanished.

The risk of hydrocephalus developing in a baby who has hemorrhaged is substantial. But with the knowledge about brain hemorrhages that medical technology has provided in recent years, Dr. Krishnamoorthy said he can reassure parents when the area of bleeding is small. "The kids tend to do okay," he said.

One day while addressing a medical meeting (Grand Rounds) on neonatal care, Dr. Krishnamoorthy presented Allison and Brook Hooper, 2-year-old twin sisters. Following premature birth, Allison suffered a hemorrhage, then hydrocephalus.

At the age of two weeks, she underwent surgery for installation of a shunt to drain excess spinal fluid from her brain to her abdomen.

At the Grand Rounds the twins looked so much alike it was difficult to tell which had the operation.

Under the Newborn Intensive Care Follow-up Program, parents bring their children to a clinic in the MGH Ambulatory Care Center initially 6 to 12 weeks following hospital discharge and at regular intervals thereafter.

A staff nurse from the ICU, Nancy Zander, RN, records each child's home progress and advises parents on common problems, such as feeding. A Pediatric Resident provides a general physical checkup, and then Dr. Krishnamoorthy conducts a thorough neurological examination.

Any patient appearing to have a developmental problem is referred to Dr. Kuehnle. She also sees all children at preschool age, 4 or 5 years, to assess their intelligence, motor strengths, perceptual skills, memory capabilities, social maturity, and behavioral traits.

The follow-up program for each child is open-ended. Dr. Krishnamoorthy, who with Dr. Kuehnle is an Instructor at Harvard Medical School, said the patient visits will continue as long as necessary to ensure that each ICU grad will grow up as normal as possible.

Although lung, heart, and brain disorders constitute the main afflictions seen in a newborn ICU, the staff also cares for a number of infants needing surgery to repair otherwise usually fatal congenital defects such as blockages of an esophagus or intestine.

Dr. David Todres, Director of the Pediatric and Newborn ICUs, said that despite the medical advances of the past decade many surgical techniques today are no different than they were 20 years ago.

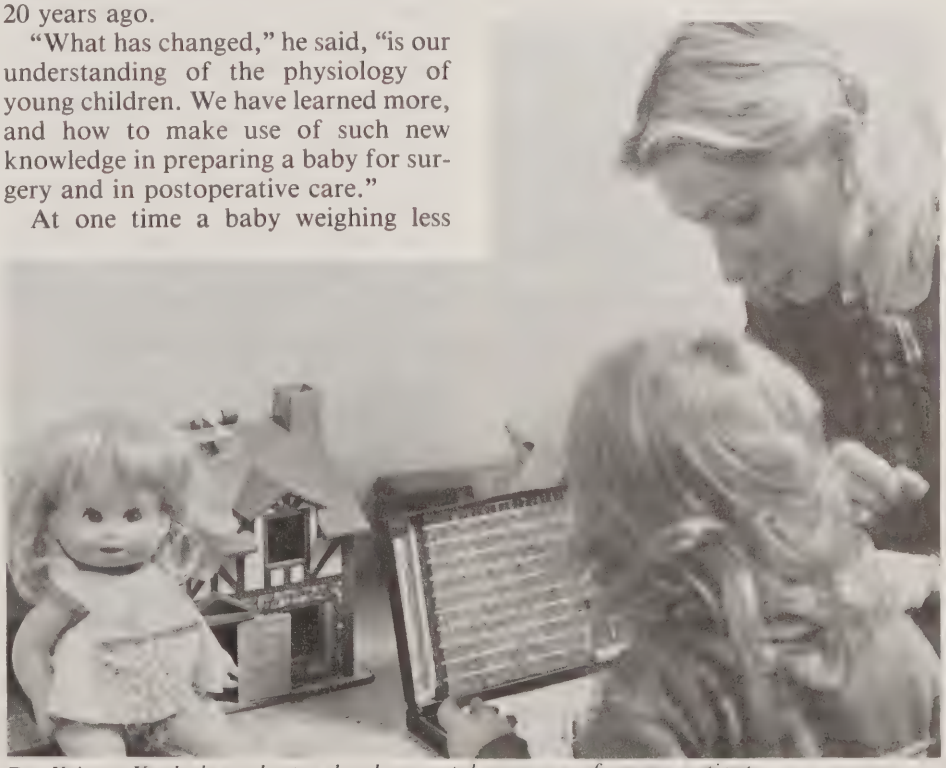
"What has changed," he said, "is our understanding of the physiology of young children. We have learned more, and how to make use of such new knowledge in preparing a baby for surgery and in postoperative care."

At one time a baby weighing less than 3¼ pounds was considered to have a very low birth weight. Today, as a result of better chances for survival, these children have been reclassified. "Very low birth weight" now applies to an infant under 2¼ pounds.

"Survival of a newborn tipping the scales at under 1⅔ pounds would still be very unusual," said Dr. Todres, an Associate Professor of Anesthesia (Pediatrics) at Harvard Medical School, but he added:

"Very often, situations that look ominous work out better than expected. Even after a serious insult to the brain, it's amazing how well a baby can recover."

Personnel in both the Pediatric and Newborn ICUs aim their efforts not just at saving a child's life but also at saving the child for a good life. ■



Dr. Kristen Kuehnle evaluates developmental progress of young patient.

Many Indoor Plants Harmful to Children

(Continued from Page 5)

tions that are not only painful but potentially life-threatening.

In a warm home, the leaf and berry stalks of holly and mistletoe may dry quickly, become very brittle, and shed freely. Adults must take great care that small children do not consume the tempting berries.

Ingestion of mistletoe berries can lead to acute gastroenteritis and, in extreme cases, even cardiovascular collapse because of digitalis-like effects on the heart. One or two mistletoe berries are sufficient to cause toxicity in a youngster.

As for holly berries, they can produce vomiting, diarrhea, stupor, and decreased function of the central nervous system. Twenty to thirty berries swallowed by a child can be lethal.

All parts of the popular poinsettia plant contain a milky sap which is very irritating. If swallowed, it can cause not only gastroenteritis but also a swelling and blisters in the mouth and throat. External contact with the skin may result in mild to severe dermatitis.

"Parents should exercise extreme caution not only with Christmas plants but also many other plants normally taken indoors because of the season's cold weather," stressed Dr. W. David Watkins, an MGH anesthesiologist, who also holds a Ph.D. in toxicology.

The list of such poisonous plants runs long, but here are a few and the hazards they pose when ingested:

Autumn crocus . . . Burning pain in the mouth, intestinal pain, vomiting, diarrhea, reduced pulse, coldness of extremities, and prostration;

English ivy . . . Excitement, labored breathing, diarrhea, and coma;

Oleander . . . Vomiting, stomach pain, abnormal heart beat, and coma. A single leaf is potentially a lethal dose for an adult;

Rhododendron, azalea . . . Vomiting, staggering walk, convulsions, difficulty in breathing, and collapse;

Philodendron . . . Burning sensation in mouth and throat. Death may result from blockage of windpipe due to swelling of soft tissues.

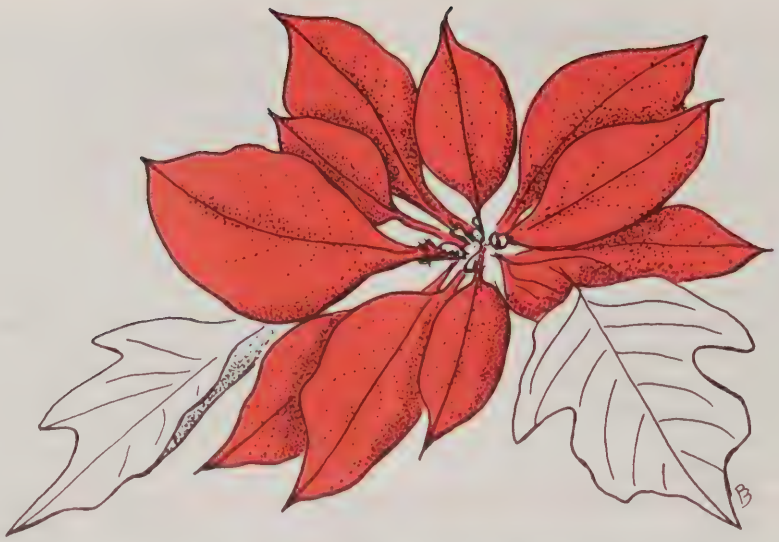
Dr. Watkins pointed out that in addition to plants Christmas tree ornaments present a danger if swallowed.

"Angel hair, a finely spun glass commonly used as a decoration, can irritate the eyes, skin, or GI [gastrointestinal] tract," he said. "Tinsel and so-called icicles can block the airways or GI tract. And snow sprays, which intrigue many children, contain methylene chloride and freon propellants.

"Prolonged exposure to methylene chloride can lead to fainting spells, nausea, headaches, and irritations of the eyes and lungs. As for the freon, it is a heart muscle irritant."

Keeping small children away from Christmas tree fertilizers and so-called "tree saver" products is vital. These products contain nitrates, and if enough is ingested, a condition called methemoglobinemia may develop.

"What happens," said Dr. Watkins, "is an alteration of the chemical properties of hemoglobin. It can no longer effectively carry oxygen in the blood, and the result can be described as a 'chemical strangulation' of the body.



Poinsettia sap can cause both internal and external problems.

The white berries of mistletoe are particularly toxic.

"Physicians should consider the possibility of methemoglobinemia in any infant who has unexplained cyanosis [a bluish discoloration of the skin]."

On festive occasions alcoholic beverages tend to flow more freely. This can create a potential hazard for small children who might gain unnoticed access to a liquor supply. Children are very susceptible to an abnormal drop in blood sugar levels (hypoglycemia) after ingesting alcoholic beverages.

Foods of a spicy nature should be kept out of tiny hands. Peppers, for instance, can irritate the eyes, nose, mouth, and GI tract of an infant. Consumed in sufficient amount, nutmeg can cause a child to hallucinate and to experience cardiovascular disturbances.

"Being a time of hurried excitement in homes, the holiday season is especially an occasion to make sure that medications are safely put away," said Dr. Watkins, who is also Associate Professor of Anesthesia at Harvard Medical School.

"The same holds true," he said, "for such common items in the home as silver, copper, and brass cleansers, detergents, glue, paint removers, drain openers, and shoe polish."

Unless proper supervision is provided, little children should be kept away from toys having components small enough to shove into the mouth. If swallowed, the parts of some construction sets, for example, could easily block a child's airways.

The inflationary rise in heating costs has created a trend which imposes greater responsibilities on householders. More and more Americans are turning to wood stoves and portable kerosene or electric heaters.

The inquisitiveness of a child at-

Although many cold medicines are advertised, they can only ease the discomfort of the illness.

Only Patience Cures the Common Cold

Whenever someone contracts a cold, nine times out of ten he is offered not only sympathy but one or more suggested "cures" as well.

They may range from aspirin, fluids, and bed rest to a mustard bath and "carrying a buckeye [horse chestnut] in his right rear pocket."

Take your pick. Regardless of which suggestion you choose, the cold, if uncomplicated, will be gone in anywhere from four to ten days.

"The fact is one cannot do anything to speed up or change the course of a simple common cold," said Dr. Cyrus C. Hopkins, a member of the MGH Infectious Disease Unit and the hospital's epidemiologist.

"All one can do is try to ease the discomfort of the symptoms until the cold ends."

In addition to using aspirin, Americans spend more than $735 million a year for other over-the-counter preparations in an effort to reduce a cold's effects.

The blow to the nation's economy in terms of lost time and wages adds up to several billion dollars a year.

The most prevalent of diseases, colds strike people of all ages, particularly children. School children average 10 colds a year, twice as many as adults. Preschool youngsters seem to be even more susceptible.

The difficulty in dealing with colds stems from the fact that they are caused by a great variety of viruses. Rhino viruses (denoting relationships to the nose) account for about half of all common colds, but even this one class of virus has some 100 strains.

Colds have a short incubation period, only 2 or 3 days. Affecting the upper respiratory tract, the illness is marked by a stuffy or runny nose and, depending on the virus, an itchy or scratchy throat, sometimes with a bit of a cough.

"The more prominent the cough, the longer it lasts, and the more sputum is produced," Dr. Hopkins said, "the more we may think of involvement of the trachea [windpipe] and the bronchial tubes, the airways leading to the lungs. Such involvement may sometimes be due to secondary bacterial infection."

Since the symptoms of colds are freqently indistinguishable from those of allergic reactions, the doctor added, it becomes important to know under what circumstances a person, especially an adult, appears to suffer from recurring colds.

About two percent of patients with colds also endure middle ear infections (otitis media). The problem arises when an inflamed mucous membrane causes a blockage of the eustachian tube, a canal leading from the middle ear to the throat. The tube's purpose is to insure the same air pressure inside the eardrum as in the atmospheric environment.

One of every 200 patients with an upper respiratory infection also develops a secondary complication of sinusitis, an inflammation in one or more of the four types of sinus cavities (frontal, ethmoid, maxillary, and sphenoid) which surround the nose (*MGH News,* November 1982).

Because of the cold, the mucous membrane lining the nose may swell to the point of blocking the passages which drain into the nose from the sinuses. Sinusitis may be suggested by persistent or worsening pain over the sinuses or in the head. Bacteria may then secondarily infect the sinuses and require a different form of treatment, including antibiotics. Antibiotics should *not* be used for the uncomplicated cold.

Colds are generally distinguished from influenza, which may cause similar symptoms but with somewhat more cough or generalized symptoms (*MGH News,* October 1978). Proper diagnosis of influenza may require a formal laboratory analysis of the offending organisms. Characterization of all respiratory viral infections as "the flu" is

(Concluded on Page 8)

tracted to an electric heater raises the specter not only of direct burns but also of electrocution if simultaneous contact is made with water or pipelines.

The burning of wood and kerosene requires proper ventilation to avoid the danger of carbon monoxide poisoning.

With regard to carbon monoxide, the increased use of automatic garage doors necessitates a few words of caution.

Dr. Watkins said some people have formed the bad habit of driving into their garage and pushing a button to close the garage door before turning off their car's engine. Any distraction such as reaching for bundles in the automobile before shutting off the motor could allow a dangerous buildup of carbon monoxide.

"Avoiding home accidents that can endanger a life is often just a matter of taking simple precautions," Dr. Watkins declared. "Also, emergency telephone numbers, such as those of the police and fire departments, family doctor, local hospital, and nearest poison information center should be readily available." ■

All parts of the autumn crocus are intensely poisonous.

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Hand Washing Helps to Prevent Colds

(Concluded from Page 7)

inappropriate since the pattern of infection is quite different.

Unlike colds, influenza tends to infect both the upper and lower respiratory tracts. Fever is also a feature of the flu whereas an elevated temperature would be unlikely in an adult fighting a cold. Fever would not be unusual, however, in a child with a cold.

People have long tried to associate the contraction of a cold with exposure to frigid weather. To refute this, the story is often told of the visit by a group of explorers to an Eskimo settlement in the far north. They could not find a single inhabitant with a cold. But some of the visitors themselves had colds, and before long the virus had spread through the entire village.

One reason why people catch colds may be that on wintry days they spend hours in overheated homes and offices, breathing air containing a low humidity. The result is that the nasal membranes dry, which may make them less resistant to germs, and confinement in a closed space with other people with colds may help transmit infection.

"Viruses may be spread by many different routes, but the epidemiology of the most common cause of the cold, the rhino viruses, is now better understood," said Dr. Hopkins, who is also Assistant Professor of Medicine at Harvard Medical School. "It seems clear that these viruses are largely spread by direct physical contact. The hand touches objects or other persons in a room, then comes into contact with the face."

A virus, he said, can live for several hours on an outside surface, such as a table top or doorknob. Therefore one of the most effective ways to avoid a cold is to pay careful attention to the cleanliness of one's hands after being in a place where germs might circulate.

Dr. Hopkins said that in general colds follow a seasonal pattern, but one cannot assert that all cold viruses occur mainly in the winter. There may in fact be different seasonal patterns for many of the different viruses involved.

Since a cold runs its course in just a few days, treatment usually consists of rest; fluids, such as fruit juices, tea, or water, to prevent dehydration; and aspirin or acetaminophen to relieve any muscle aches and pains, headache, or fever.

In children, however, aspirin should not be used in respiratory infections without discussing it with a doctor since there may be an association between aspirin use for certain infections and the subsequent development of Reye's syndrome, a serious and life-threatening disease of the liver and brain.

A decongestant, taken orally or in spray or drop form, can be very helpful to cold sufferers with a tendency to develop sinus or ear complications.

"We tend, however, to recommend decongestants only for the acute short-term care of the cold," Dr. Hopkins emphasized. "Overuse of a nasal spray, for example, may lead to a so-called 'rebound' phenomenon whereby tissues that initially shrank subsequently swell and become even more congested."

A virus can live for hours on an outside surface such as a telephone.

Investigators in England have conducted extensive trials to determine whether interferon, a natural antiviral substance produced by the body, can prevent colds.

Tested against a single virus, pure interferon, made in a laboratory, reportedly showed that it can under certain circumstances offer virtually complete protection.

Other preliminary research indicates interferon would have to be used frequently and in high doses. Since its cost is extremely high, practical use of the substance against colds may lie far down the road. With new gene splicing techniques, however, the artificial mass production of interferon may shorten that road considerably.

Much controversy exists over the value of vitamin C as a cold fighter. Some people have suggested that doubling the normally recommended intake of vitamin C can slightly reduce the severity of a cold. More than doubling the dosage though, they said, would offer no added advantage.

A number of investigators believe any benefit emerging from use of the vitamin is really a placebo effect; that is, it only makes the patient incorrectly believe that he is benefiting.

"I personally don't know of any solid evidence thus far that vitamin C protects people from colds," Dr. Hopkins declared.

In considering treatment of a cold, the MGH specialist offered a final suggestion:

"Many anticold remedies are bought over-the-counter in capsule form. Because of recent instances of tampering, it seems prudent to be cautious in considering purchase of capsules until the preparations come in packages with tamper-resistant seals." ■

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 42 No. 1 January/February 1983

Specialists Save Young, Critically Ill Heart Patient

Adults Must Realize The Body's Need For Vitamin D

In the days when countless children began life in dark and dingy tenements and in early years labored long hours in sunless factories, the most common nutritional disease in childhood was rickets.

Brought on by a deficiency of vitamin D — the so-called sunshine vitamin — the disease caused defective and frequently crippling bone development. One consequence was a high infant mortality rate at birth because of a deformed pelvis in the mother.

Daily spoonsful of cod liver oil plus use of milk and other dairy products fortified with vitamin D, and the advent of mass-produced vitamins combined to reduce childhood rickets in the United States to a "medical rarity."

But the problem of rickets has not ended. Adults also fall victim to the illness. In their case, it is referred to as osteomalacia (a softening and demineralization of bone).

The disease, which increases adult susceptibility to fractures, principally affects two groups: (1) those whose body machinery for activating vitamin D has failed, and (2) individuals who because of advancing years cannot make enough of the vitamin in their skin.

Studies indicate that tens of thousands of Americans suffer from osteomalacia because of poor vitamin D nutrition or the vitamin production slowdown caused by aging.

At the MGH and other medical centers, investigators are striving to find more efficient ways of overcoming vitamin D deficiencies and, in general, to gain a better understanding of this substance, which in its active form is really a hormone.

A vitamin is a necessary nutrient that cannot be made by the body and therefore is provided by the diet. In contrast, a hormone is produced in body tissue. The hormone then travels through the blood stream to another tissue to promote a biologic action.

Vitamin D is unusual in that it can either be made in the body or provided in the diet; hence, it has characteristics of both a vitamin and a hormone. However, the material becomes active in the body only after biochemical transformations. The transformed, or activated, form of the molecule is made by the body in response to physiologic

(Continued on Page 2)

Three-year-old Isabel Gutierrez during a postdischarge hospital visit with her mother

When Dr. Richard R. Liberthson first examined 3-year-old Isabel Cristina Gutierrez in September, he doubted that he had ever seen a sicker child.

Brought from her home in Cali, Colombia, to see the MGH heart specialist, Isabel was so weak she was unable even to lift her head on being carried into his office.

Afflicted with heart problems which had also damaged her liver and a kidney, the child was emaciated. She had not eaten for several weeks, save for minimal amounts of a special milk formula fed to her by the teaspoonful. Her skin exhibited a bluish hue, a sign of inadequate oxygen in her blood.

Dr. Liberthson found that Isabel was suffering from cardiac cathexia, a condition denoting such extreme heart failure that all of the calories she consumed were being used just to keep her heart beating. The rest of her body was wasting away.

Her visit with Dr. Liberthson marked the beginning of a 2½-month stay at the MGH during which at least a dozen specialists, backed by teams of nurses and other support personnel, fought to save the child's life. All of the physicians and surgeons who became involved provided their services without charge.

At the end of her hospitalization, Isabel was a "new person," to quote her mother, Mrs. Ali Gutierrez. "I can't believe this is true," she told Dr. Liberthson.

Isabel eats well now. Her bluish skin tone has gone. And she walks with other children.

Dr. Liberthson said she will be able for the first time to keep up with her twin, Maria Clara. "Isabel can look forward to a normal, or at least near-normal, life," the MGH cardiologist

(Continued on Page 4)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114 Telephone (617) 726-2206

Martin S. Bander	*Editor*
Myron H. Daniels	*Assistant Editor*
Doris G. Schreckengaust	*Copyreader*

EDITORIAL BOARD

J. Robert Buchanan, MD	*General Director*
Kurt J. Isselbacher, MD	*Research, Medicine*
Paul S. Russell, MD	*Surgery*
Ronald A. Malt, MD	*Surgery*
Roger H. Sweet, MD	*Utilization*
Stanley Bennett	*Photography*
Robert J. Galla	*Design*

EDITORIAL:

Teaching Hospitals Serve As Magnet

Teaching hospitals are expensive. They also provide outstanding care. For a difficult to diagnose or treat problem, they usually represent the only hope. By reputation Boston is often considered America's medical solar system with the teaching hospitals its sun.

Boston's hospitals attract to Massachusetts tens of millions of dollars each year for medical research. That research brings the best investigators and the best physicians. Often the fruits of the research give patients in these teaching institutions the most advanced care in the world. And those millions of dollars in outside research funds provide significant income for Massachusetts residents.

The word "teaching" implies the education of medical students and the training of interns and residents. With three major medical schools in Boston and a fourth nearby in Worcester, Massachusetts offers an unusual concentration of medical education. Like research, the medical schools act as a magnet to draw the best physicians. Bright young minds challenge experienced physicians and stimulate them to new heights just as a laser stimulates coherent particles of light.

The benefits of teaching and research at the Boston hospitals also accrue to community hospitals in Massachusetts and everywhere. Ultimately the research is brought to a variety of institutions. Similarly, physicians who train in Boston often care for patients in other cities.

It is little wonder then that Boston hospitals provide the quality of care they achieve. It is no wonder that patients do travel the world to seek out Boston hospitals. Nor is it any wonder that Massachusetts industry extolls Boston's teaching hospitals when enticing employees to Boston. Or that Massachusetts politicians use the lure of the Boston hospital in attracting new business. Interesting that businessmen and legislators combined to force cost control legislation on these very hospitals. Will the long-range result be that businessmen and politicians will one day have little left to praise?

The Sun's Energy Limits Vitamin D Output in Skin

(Continued from Page 1)

needs, and thus is a true hormone.

The beneficial effect of sunlight in both the treatment and prevention of rickets and osteomalacia has been recognized for more than 60 years. But only in recent times have doctors learned how the body makes vitamin D.

Much of the increased knowledge resulted from work conducted since 1969 by Dr. Michael F. Holick, who earned master of science, Ph.D., and MD degrees from the University of Wisconsin.

While a graduate student there, he developed the first oral form of activated vitamin D that subsequently aided tens of thousands of patients suffering from kidney failure and related bone disease. His research was the subject of his Ph.D. thesis.

Dr. Holick joined the Endocrine Unit at the MGH in 1975 as a Research Associate and started the hospital's Vitamin D Laboratory that same year. In his studies that followed, the pieces of the vitamin D puzzle gradually fell into place.

Dr. Holick and his colleagues showed that upon exposure to the sun a precursor to cholesterol found mainly in the epidermis, or outer layer of the skin, converts into a previtamin D. Over the next two or three days the previtamin turns into vitamin D, still in its inactive form.

A protein in the blood with an affinity for vitamin D then transfers the substance into the circulation for transport to the liver to become 25-hydroxyvitamin D, still inactive.

It is not until the production line carries the 25-hydroxyvitamin D from the liver to the kidneys to become 1,25-dihydroxyvitamin D (Calcitriol) that the body finally gets the working form of the hormone.

What controls the production assembly line? Apparently solar energy limits the output. Dr. Holick's team found that after sufficient hormone is made, ultraviolet light will cause previtamin D to break down into biologi-

Photographs: Pages 1, 3, 4, 5, 8 (lower), Myron Daniels; p. 6 (upper), courtesy of Dr. John Fallon; p. 6 (lower), courtesy of Drs. H. William Strauss and Kenneth McKusick; p. 7 (upper), courtesy of Dr. Majic Potsaid; p. 7 (lower), courtesy of Dr. Arthur Weyman.

Drawing: Page 8 (upper), courtesy of American Heart Association.

cally inactive compounds.

"If a Caucasian were exposed to sunlight in the tropics for 15 minutes or so, he would convert 10 or 15 percent of his cholesterol precursor to previtamin D," said Dr. Holick. "Further exposure would only lead to inert products."

Dr. Holick's studies helped to explain why dark-skinned people, especially those living in cold, northern climates, suffer more from vitamin D deficiency.

"Melanin [a dark pigment found in skin] competes for the ultraviolet light that enters the skin and therefore inhibits the production of previtamin D," the doctor explained.

"In heavily pigmented individuals, it takes five to 10 times more exposure to sunlight to make the same amount of vitamin D that a Caucasian will make."

To investigate the sun's effect on skin in the production of vitamin D, Dr. Michael Holick uses an artificial light source that mimics the sun's ultraviolet rays.

"As one ages the ability to make vitamin D clearly decreases."

Even though vitamin D is added to the diet in the United States, Americans are known to undergo a decrease in bone mass as they advance in years; women after 40, men after 50. Dr. Holick sought to learn whether aging had any effect on the capacity of the skin to make vitamin D.

The research led to a conclusion that "as one ages the ability to make vitamin D clearly decreases."

"A 20-year-old person has about twice the amount of the cholesterol precursor as a 60- or 70-year-old," said Dr. Holick, who is Associate Professor of Medicine at Harvard Medical School and Associate Professor of Nutrition and Food Science at Massachusetts Institute of Technology. He is also Associate Director of the Clinical Research Center at M.I.T.

Since many older people subsist on unsatisfactory diets, Dr. Holick believes it is important for the elderly to get some exposure to the sun and produce vitamin D in their skin, or to take vitamin pills containing the recommended daily allowance of 400 International Units (10 micrograms) per day.

"Exposure of the face and arms to the sun for 10 or 15 minutes a few times a week in the summer is probably adequate to maintain proper vitamin D levels in Caucasians during that season of the year," he said. "A dark-skinned person would, of course, need more time in the sun."

Being a fat-soluble substance, vitamin D can be easily stored in the body to meet its needs for several months.

In the MGH Vitamin D Laboratory, Dr. Holick and his team are trying to develop a way of supplying the activated vitamin D in the form of a cream or ointment spread on the skin.

Already incorporating transformations that normally take place in the liver and kidneys, the cream would be converted to activated vitamin D by exposure to the ultraviolet rays of sunlight or by ultraviolet phototherapy. Once absorbed through the skin into the blood, the hormone would proceed directly to the intestines to begin its biological function of regulating the amount of calcium absorbed from the diet. The supplement would also go to the bone to control release of calcium into the blood.

Trials with volunteers have supported the concept of a topical treatment and have been described in the New England Journal of Medicine. *Dr. Holick cautioned, however, that such a therapy can be years away.*

"Although we've shown that we can use the skin as site for the synthesis [manufacture] and absorption of the active form of vitamin D in human volunteers," he said, "we are only getting about one to four percent of the drug through the skin. We'd like to develop a method that would permit 40 to 50 percent of the hormone to penetrate the skin."

(Concluded on Page 4)

A high pressure liquid chromatograph, demonstrated by Research Technician Nancy Hanafin, determines components of vitamin D in a blood sample so that the quantity of each component can be established.

Colombian Girl Beset With Multiple Defects

(Continued from Page 1)

said. The twins also have a 5-year-old sister, Sofia Margarita.

When Isabel was born in Cali, doctors realized immediately that she had a complex form of heart disease. Called "tetrology of Fallot," the malady consisted of four heart defects: a narrowing of the pulmonary artery which carries blood from the right ventricle, or pumping chamber, to the lungs to pick up oxygen; a hole in the wall separating the right and left ventricles; an enlarged right ventricle; and an overriding main artery (aorta) (*MGH News,* November 1980).

"In the United States, a child with such problems would undergo surgery early," Dr. Liberthson said, "but in many parts of the world where programs in cardiology and cardiac surgery are just developing, it is not unusual to delay operations until a child is older so as to minimize the risks."

Early last spring, Isabel's father, an engineer with the Colombian government, arranged for the necessary surgery at a midwestern hospital. Major complications, including a stroke and an infection of the chest and heart, prolonged the hospitalization by about two months.

The infection so weakened the girl's heart that after returning home she could not undergo even minor procedures without risking severe heart fail-

Isabel could not help being shy even with her MGH friends, including (from left) Dr. Richard Liberthson; Surgical Intensive Care Unit nurses Mimi O'Donnell, Patricia Wolfe-Barnett, and Cheryl Oliver; and, in right rear, Dr. Eric Hanson, Chief Resident in Cardiac Surgery.

Vitamin D

(Concluded from Page 3)

Dr. Holick envisions wide appeal for treatment through the skin *if existing obstacles can be overcome.* The hormone would be released slowly into the blood stream, thus decreasing the risk of toxicity, such as high levels of calcium in the blood and urine, that oral dosage might cause. Also, application of the salve or ointment might be necessary only once a month, compared to a daily pill requirement.

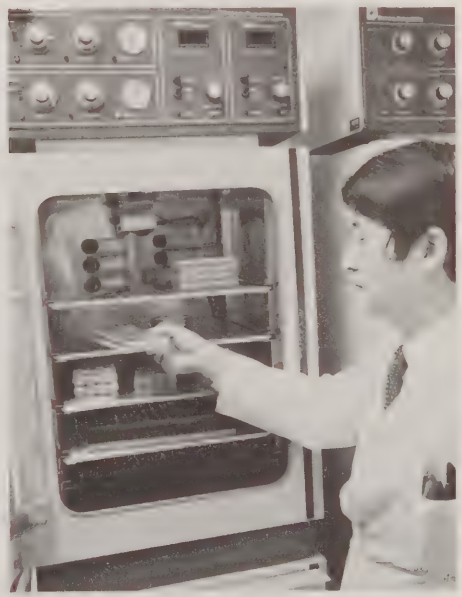
As Dr. Holick continues with his vitamin D studies, exciting new challenges arise.

"There have been findings that the active form of vitamin D not only goes to the bone and intestine but may also have biologic roles in organs that we never thought came under the hormone's influence," he said. "The pancreas, pituitary gland, ovary, and skin, just to name a few of the organs, appear to each have a receptor for this hormone.

"Furthermore, a Japanese group has recently demonstrated that incubation of certain mouse and human leukemic cells with the active form of vitamin D caused these cancerous cells to become normal."

The concept that vitamin D might one day have a role in curing leukemia is exciting, Dr. Holick admitted, but he cautioned that vitamin A also is quite potent in causing cell changes and to date "vitamin A has not been very effective as an antitumor agent."

The possibility of such uses for vitamin D, nevertheless, has spurred very active investigations. ■



A skin cell culture being used in the study of vitamin D metabolism is placed in an incubator by Dr. Masaaki Fukase.

ure and possible death. She was bedridden, could hardly eat, and was slowly wasting away.

The family learned of Dr. Liberthson through his involvement with cardiology programs at the University of Cali Medical School and the Colombian public health system. He has been working with both of these groups to further the development of their diagnostic and treatment programs for heart patients in Colombia's second largest city.

Although he lectured there only last spring and had heard about a very sick child, he did not meet her until a resident of Scituate, Mass., who does business in Colombia, telephoned the MGH heart specialist in Boston. Isabel and her mother were here, Robert King said. Can you see them?

Because of Isabel's critical condition, several specialists had to be summoned before Dr. Liberthson could even schedule a cardiac catheterization

Cardiac Technician Concetta DeRosa prepares Isabel for an electrocardiogram test to check the electrical activity of her heart.

. . . The child's lungs were continually filling with fluid because of her heart failure.

whereby a tube, or catheter, is extended through a blood vessel into the heart for tests to define the exact nature of abnormalities.

Isabel's liver function and blood-clotting factors were so abnormal that Dr. Paul R. Harmatz of the Pediatric Gastrointestinal Unit and John T. Truman of Pediatric Hematology–Oncology were called in.

Abnormal kidney function brought Dr. John T. Herrin of the Renal Unit. And Dr. G. Robert DeLong of Pediatric Neurology evaluated Isabel's neurologic status in view of her earlier stroke. He found that she had overcome that problem. Subsequently, Dr. Igor Palacios performed the cardiac catheterization.

A gloomy picture emerged from the various tests and procedures: Isabel's infection had torn loose the patch that closed the hole in the wall separating the two heart ventricles. The tricuspid valve between the right atrium, or blood collecting chamber, and the right ventricle also had torn.

The result was such a severe backup pressure that the liver became enlarged and could no longer function properly. The pressure also dilated and obstructed the drainage of a kidney, necessitating surgical revision of the tube draining this kidney. Dr. Samuel H. Kim of pediatric surgery performed this procedure.

Even as physicians were preparing Isabel for critical heart surgery by Dr. Mortimer J. Buckley, Jr., Chief of the Cardiac Surgical Unit, the child's lungs were continually filling with fluid because of her heart failure.

Despite high risk, Dr. Buckley went ahead with the operation to save her life. He repaired the torn patch between the ventricles and added another for strength. He put the tricuspid valve into workable order, and he rerepaired the pulmonary artery. Following the surgery, Isabel did extremely well but faced further procedures.

She still had a cardiac conduction problem. A structure called a sinus node, situated in one of the heart's atria, normally sets the pumping rate for the ventricles. Isabel needed a permanent pacemaker to establish and maintain a reliable heart rhythm.

A Minneapolis-based electronics firm, Medtronic, Inc., donated a pacemaker valued at more than $5,000 after consultation with Dr. J. Warren Harthorne, Director of the MGH Pacemaker Laboratory. Dr. Alan D. Hilgenberg, a thoracic surgeon, implanted the device in the child's abdomen and attached the electrodes to the heart.

Total parenteral nutrition (*MGH News,* December 1976–January 1977), a technique by which nutriments are delivered intravenously, supported Isabel until gradually she began to eat on her own more and more.

With exhaustive attention from nurses in the Surgical Intensive Care Unit on White 3A, the Pediatric Intensive and Intermediate Care Units on Burnham 6, and on the pediatric floor on Burnham 5, the youngster from Colombia grew steadily stronger.

In addition, Dr. Veronica Miller, a pediatric resident, and Dr. Robert Drucker, a pediatric renal Fellow, followed Isabel through every phase of her care until her discharge. Dr. Miller also served as the child's interpreter.

In Scituate where Mrs. Gutierrez and Isabel stayed with the King family, Mrs. Robert King was amazed at the change that the MGH care had made in the child.

"She acted so strangely and was so pathetic looking when she first came to us," Mrs. King recalled. "But after her hospital stay, she began to play with our own children, and for the first time she smiled . . . she laughed . . . she giggled."

On leaving the MGH after a final visit, Mrs. Gutierrez carried a transmitter, courtesy of Medtronic. With the device hooked to a telephone line, Isabel's cardiologist in Cali, Dr. Martin Waartenberg, will be able to send the MGH copies of the girl's electrocardiograms (ECGs), which record the electrical activity of her heart. Thus, the little girl will never be far away.

And as Mrs. Gutierrez bade goodbye to Dr. Liberthson, tears welled in her eyes:

"Papa won't recognize Isabel," she said. ■

Heart Failure Takes Many Forms

A majority of Americans who suffer heart attacks have coronary artery disease in which high blood pressure is often a major factor.

But the role of hypertension in heart failure — the leading cause of death in the United States — is much more extensive.

Mildly elevated hypertension which has gone unnoticed or untreated for many years can lead to heart failure without triggering a heart attack.

"I think the most common way in which this happens," said Dr. Robert Arnold Johnson, an MGH cardiologist, "is that the left ventricle, or pumping chamber, of the heart gradually thickens as the years pass. Eventually, this hypertrophy [exaggerated growth] of the muscle produces sufficient abnormality of stiffness to bring about the heart failure."

During this period of muscle thickening, the doctor added, the ventricle continues to contract normally, or nearly so.

"This is a very different situation," he said, "than when coronary artery disease causes heart failure by means of a myocardial infarction [heart attack], yet a very common situation, perhaps nearly as common a cause of heart failure as is a myocardial infarction."

Heart failure refers to a backup of pressure in the veins as a consequence of high pressure in one or both of the heart's atria, or blood-collecting chambers.

In so-called left heart failure, which is most common, pressure backup causes fluid from the blood to enter air sacs of the lungs, making breathing difficult.

The advent of echocardiography a decade ago (*MGH News,* September 1980) and gated cardiac blood pool scanning, a nuclear medicine technique, enabled physicians to measure heart contraction and discover that muscle stiffness was the reason for heart failure in many patients.

Enlargement of the left ventricle because of poor contraction and poor ejection is the most common mechanism by which a heart attack brings on failure. Aortic-valve obstruction (calcification) can produce heart failure by this means.

Overindulgence in alcohol, or many other causes of heart-muscle disease, can produce the same course without a heart attack necessarily occurring.

An inner view of a heart triple its normal size because of muscle disease

Other potential causes of left heart failure:

• A ventricle which ejects normally but becomes enlarged due to excessive blood entering the chamber. Valvular regurgitation, severe anemia, heat stroke, a deficiency of Vitamin B_1, or an abnormal connection between an artery and a vein (arteriovenous fistula) might cause the ventricle to enlarge.

• Stiffness of a ventricle from a cause other than hypertrophy. Infiltration by tumor or deposition of an abnormal protein (amyloid) are examples.

• Obstruction of the mitral valve which connects the atrium and the ventricle, such as mitral stenosis, a common form of rheumatic heart disease.

• A blockage in the atrium itself, such as by a tumor.

In at least a third of patients with left-sided heart failure, the right side also ultimately becomes involved, resulting in systemic venous hypertension and swelling in parts of the body, such as the ankles. Why left heart failure becomes bi-sided in some patients is not possible to explain in many instances.

Right-sided failure can occur alone. "In most instances, this is due to obstructive airways disease resulting from cigarette smoking," said Dr. Johnson. "Other patients may have pulmonary emboli [floating clots in blood vessels of the lung]. Since only the lung arteries are involved, only the right heart sees the abnormality."

In treating heart failure, a physician most commonly begins by administering a diuretic drug. This causes more of the blood's fluid to be excreted as urine. The amount of blood returning to the heart is thus diminished, and pressure in the atria falls.

"If the patient is extremely short of breath and in severe distress, then morphine is often given," Dr. Johnson said. "When given intravenously, morphine works extremely fast to calm anxieties, which are a major component of the problem, and to speed resorption of fluids by reducing pressures in the lung veins."

When administered in sufficient dosage, nitroglycerin and a number of other drugs that expand blood vessels have an effect similar to morphine.

Doctors sometimes prescribe medication to improve the strength of contraction of the heart. Between four and five million Americans, for example, take digitalis or a derivative. The drug

Using a scintillation camera and a computer, nuclear medicine and cardiology specialists obtain images showing the heart most filled with blood (left) and fully contracted (right). Doctors can then assess the size and function of the heart's major chambers.

increases the strength of contraction sufficiently to cause a reduction in heart size in some but not all patients. Those whose left ventricle is greatly dilated respond best to digitalis. The diastolic, or resting, pressure of the heart falls and, in turn, atrial pressures become lower.

Other drugs can be used to accentuate the contractile vigor of the heart, but none are used as commonly as digitalis and its relatives.

Although many forms of heart failure result in an accumulation of fluid in the lungs (pulmonary edema), death from that condition is relatively uncommon nowadays because it is almost always treatable.

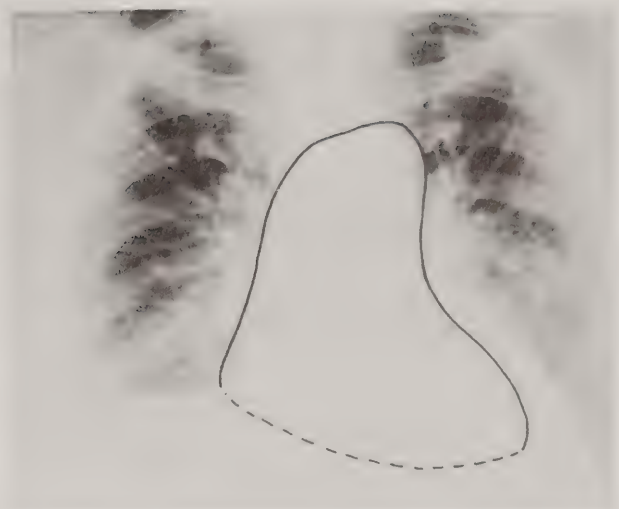
For the most part, death from heart failure is due to a long-term complication, such as starvation of the heart from not enough blood being pumped per minute or an abnormal heart rhythm.

Patients most at risk, Dr. Johnson said, are those whose ventricles are not ejecting normally. They usually have disease of the heart muscle itself. Patients with heart failure from stiffness of the ventricle seldom die from this condition because the backup pressure is reversible and the amount of blood being pumped is normal, or nearly normal.

Some patients develop heart failure because their heart pumps too much blood.

"Such patients almost always have a condition that can be corrected through surgical repair of a valve that might be leaking or by treatment of an underlying disorder such as anemia," said Dr. Johnson, who is also Assistant Professor of Medicine at Harvard Medical School.

While surgery attacks the basic problem, medicine only treats the consequences of a heart malady. The cost of relieving symptoms by drugs may be higher in terms of their effect on lifestyle than the patient expects.



Chest X ray showing an enlarged heart

Superimposed outline depicts normal heart size.

Although diuretic drugs may eliminate the symptoms of congestion, they may also have side effects, for example, in the form of fatigue, allergies, or a need for potassium supplements.

When bi-sided heart failure exists, doctors prescribe more diuretics. This often necessitates an anticlotting drug such as Coumadin because right heart failure predisposes to clotting in leg veins and to pulmonary emboli.

Drugs that expand blood vessels may affect blood pressure to a degree that the patient gets dizzy upon arising from a chair or a bed. Sometimes the drug can be changed or its dosage altered, but more often the patient copes with the situation by adopting new habits. Thinking ahead and getting up slowly may be all that is necessary to prevent the dizziness.

How much rest should a heart patient get? Since heart failure caused by hypertension is treatable, Dr. Johnson believes such patients need very little restructuring of their everyday lives.

"The question of rest should really be aimed at those individuals with conditions for which no operation is available and in which the mechanism of the heart failure is disease of the heart muscle itself," he said.

Even then, he said, no evidence exists to support a prevailing point of view that more rest, such as a daily nap, is required.

"My own approach is to ask my patients directly about this," he added. "Do they think a nap during the day might pep them up? If they think so, fine. I encourage them to try that. If they scoff at the idea, so be it."

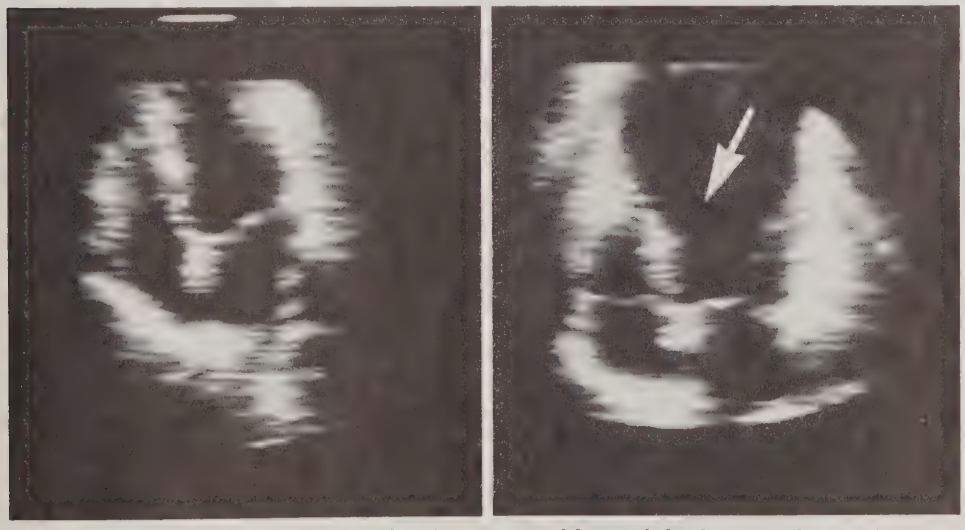
As for diet, Dr. Johnson stresses that heart patients should avoid abnormal amounts of salt which retain fluids in the body.

"I suggest doing away with the salt shaker at the table and also avoiding foods that taste salty when they're first eaten," he said. "But I don't believe it is practical to eliminate foods that contain some salt which the patient can't taste. You don't want to make food unpalatable."

Dr. Johnson pointed out that the variety of diuretics available today makes it possible to adjust diets accordingly.

"Heart failure cannot be viewed as a global condition," Dr. Johnson said. "Each time we use the term we must immediately think of the cause and mechanism. Otherwise, whatever we say will not be relevant to all.

"In some conditions causing heart failure, sudden death has an increased incidence even if the symptoms are perfectly controlled, but there may well be patients within the group who will live quite a long while." ■



Two-dimensional echocardiograms showing a normal heart (left photo) and (at right) a heart with an enlarged left ventricle (See arrow.)

Address Correction Requested

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

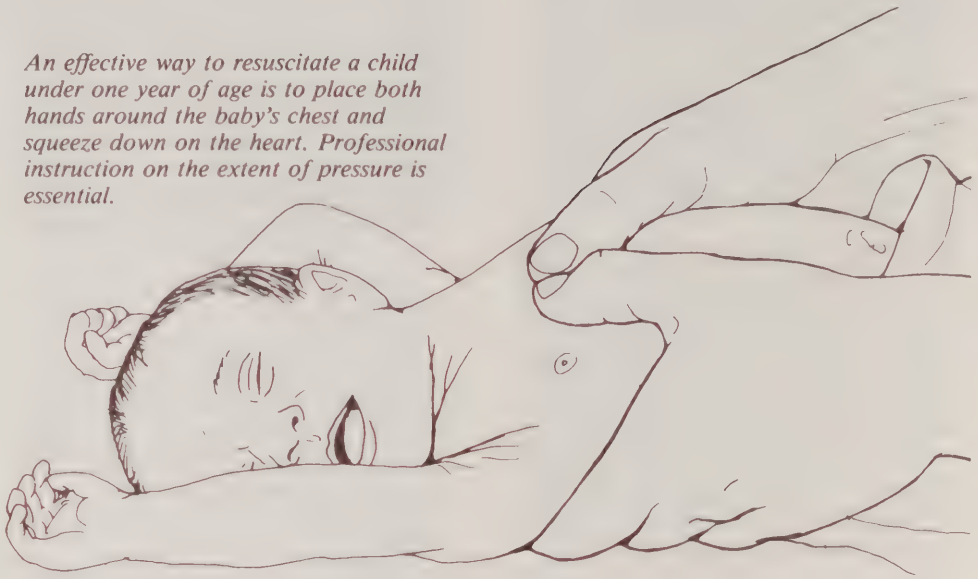
Feeling Quickly for a Little Child's Pulse

The American Heart Association is encouraging the public to adopt an alternative way of quickly discerning a heart beat in a child under 1 year of age who may need C.P.R. (cardiopulmonary resuscitation).

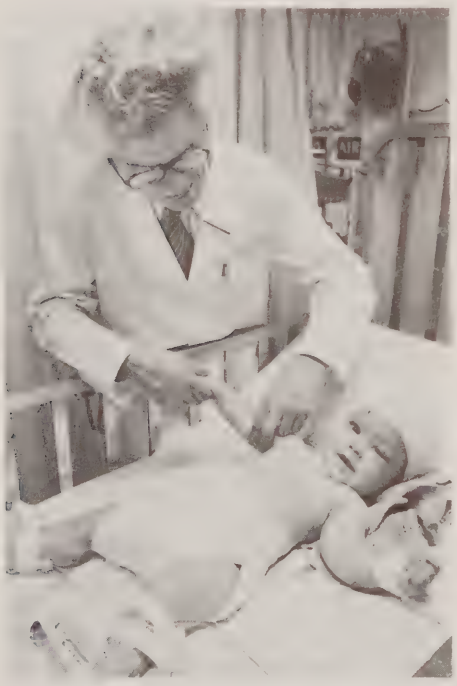
Absence of a beat would signal immediate need for externally applied compression of the heart to keep blood circulating through the body, as well as mouth-to-mouth breathing support.

To check heart function it has been customary to press a finger against one of the two carotid, or main, arteries in the neck. But a child under 1 often has practically no neck. His head virtually sits on his shoulders. So finding the carotid artery in a baby is not easy.

On recommendation of a five-member study committee, the heart association proposes feeling for a pulse in the brachial artery. That is the main blood vessel running through the arm and the one used in taking blood pressure.



An effective way to resuscitate a child under one year of age is to place both hands around the baby's chest and squeeze down on the heart. Professional instruction on the extent of pressure is essential.



With the aid of 7-months-old Jaime Oteyza of Caracas, Venezuela, Dr. David Todres shows how to detect the brachial artery pulse.

A cardiac beat can be detected by placing a couple of fingers against the inner part of the upper arm and pressing the artery against the bone.

"One can often feel the thrust of a baby's heart by placing a hand over its left chest, but this may not be so in as many as 40 percent of the infants," said Dr. David Todres, Director of the MGH Pediatric and Newborn Intensive Care Units and a member of the heart association committee.

"In the past, medical personnel also have considered the pulse in the femoral artery [in the groin] to be a good indicator of heart function in the small infant or child. But it sometimes takes a trained person to detect that pulse."

Before recommending the brachial test, the committee gathered a group of parents representing the lay public and taught them how to feel for the carotid, femoral, and brachial pulses. Then the parents and a number of physicians and nurses were timed to see which pulse they could feel most easily and quickly. The brachial won.

"Some people have suggested, 'Why not feel at two sites?'" Dr. Todres said. "The heart association rejected this on grounds that people might waste time in an emergency."

To compress the heart of an infant, you have two options. Dr. Todres said that an individual can press two fingers directly down on the breastbone, or sternum, or can place both hands around the baby's chest and squeeze down on the heart.

As for breathing assistance, if the baby is very small, an adult helper would place his mouth over both the nose and mouth of the infant for the greatest effect. And instead of major breaths, the helper would employ puffs.

An important caution: To learn C.P.R., you must do more than read about it. Professional on-the-scene instruction is required to learn to apply C.P.R. effectively and safely. ■

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 42 No. 2 March, 1983

Winning a Long Struggle to Overcome Severe Acne

Doctors Study Extent Of Viral Involvement In Immune Disorder

A member of the herpes family of viruses is coming under intensified scrutiny at the MGH to determine if the agent is important to the development of an immune disorder which has stricken close to 900 people.

AIDS (Acquired Immune Deficiency Syndrome) cripples the body's disease-fighting, or immune, system leaving the victims susceptible to a host of tumors and infections.

Three-quarters of AIDS victims are homosexual or bisexual males. Another 15 percent are drug abusers. Haitians, mainly recently arrived immigrants, account for another five percent. Less than one percent of the patients suffer from the bleeding malady, hemophilia. The remaining four percent of AIDS victims either had prior contact with other patients or bore no identifiable risk factor.

Under a grant from the National Institutes of Health, infectious disease specialists at the MGH are focusing much of their attention on cytomegalovirus (CMV) in their search for a cause of AIDS.

"It seems to be present in nearly all patients stricken with the syndrome," said Dr. Martin S. Hirsch, Director of the MGH Virology Laboratory.

His group was the first to point out that CMV has a suppressive effect on the human immune system. In 1967, Dr. Donald N. Medearis, Jr., now Chief of the MGH Children's Service, was senior investigator in a Johns Hopkins University study which showed

(Continued on Page 4)

When Brenda Stead walks into a room, men usually notice. She's that attractive. Once, they used to look away.

The 31-year-old bookkeeper from Melrose, Mass., admitted that only five years ago "it was not the most pleasant experience to be seen in public."

At the time, large, unsightly sores hid much of Miss Stead's face, extending over portions of her back and chest as well. The psychological impact was immense.

The young woman's affliction was no rare disease. Her plight stemmed from acne, a skin disorder that strikes virtually every Caucasian, usually during adolescence. Orientals and blacks are reported to contract the problem less frequently.

Miss Stead's ordeal began when she was 21, a time when the self-limited disease customarily abates. After several physicians tried vainly to help her, she was referred to Dr. Thomas B. Fitzpatrick, Chief of Dermatology at the MGH. His treatment with antibiotics and hormones seemed beneficial for a while, but then periodic flare-ups erupted.

With Dr. Fitzpatrick's assistance, the young woman enrolled in a federally funded program at the National Institutes of Health in Bethesda, Md. A researcher, Dr. Gary L. Peck, was conducting a study of a synthetic derivative of vitamin A in the treatment of cystic acne.

Although the treatment calling for pills several times a day extended over 16 weeks, positive results became apparent after only the first two weeks. Gradually the acne vanished. Even after the treatment concluded, *(Continued on Page 2)*

Brenda Stead, at left with severe cystic acne and at right some two years after completing new treatment

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206

Martin S. Bander	*Editor*
Myron H. Daniels	*Assistant Editor*
Doris G. Schreckengaust	*Copyreader*

EDITORIAL BOARD

J. Robert Buchanan, MD	*General Director*
Kurt J. Isselbacher, MD	*Research, Medicine*
Paul S. Russell, MD	*Surgery*
Ronald A. Malt, MD	*Surgery*
Roger H. Sweet, MD	*Utilization*
Stanley Bennett	*Photography*
Robert J. Galla	*Design*

EDITORIAL:

In the Rush to Control Hospital Costs

In previous editorials we have traced the hospital cost rise of the last decade and one-half. We have observed that one major factor was introduced by Congress's creation of Medicare and Medicaid. The underlying theme of those acts was quality and equality of care to the elderly, the crippled, and the indigent.

To a significant degree those laws have achieved their dual purposes. While the government asks Medicare patients to share an increasing portion of the bill, the basic premises of quality and equality have more or less remained. Those fundamental precepts are about to disappear. For along with quality and equality came cost inflation.

In Massachusetts the inflation has led to the cost containment legislation known as Chapter 372. Some believe that Chapter 372 will serve as a national model. Others believe that a New Jersey experiment based on payment for something called Diagnostically Related Groups will prevail.

In brief, this is an attempt to pigeonhole causes of hospital admissions into various related groups of diagnoses. The idea is to predetermine how much each hospital should receive per patient admission.

For someone needing a mitral (heart) valve replacement, the sum allotted might be, let's say, $9,000 regardless of length of stay. The federal government might allow slight variances for conditions in various parts of the country. What, though, about hospitals whose patients tend to have either more serious conditions or secondary problems?

The length of stay and cost of care might prove considerably greater if the person needing the new mitral valve also suffered from diabetes or even mild emphysema. Clearly reimbursement to treat such a patient would have to be considerably more.

In its original form there is no indication whatsoever that the government proposal would be anywhere near that sophisticated. Lack of that kind of sophistication would prove catastrophic to hospitals and ultimately the public.

* * * *

How do these new plans affect quality of care? In their rush to control costs, governments are no longer talking about quality. When they do mention it, they imply that quality will somehow remain high even while costs go down. Uh huh.

Acne Affects Millions In a Varying Degree

(Continued from Page 1)

healing continued. Miss Stead still remains free of acne lesions — years after treatment.

Reporting in the *Journal of the American Academy of Dermatology,* Dr. Peck described how the drug, 13-*cis*-retinoic acid (Accutane), led to complete clearing of cystic acne in 13 of 14 previously treatment-resistant patients.

Some 16 million Americans have acne. For many, the ailment means just an occasional pimple. For others, the condition may mean long-term physical and emotional scarring but terminates before the patient reaches the mid 20s.

In about 10 percent of acne patients, the malady persists beyond the usual cutoff time, but of this population not more than 30 percent have acne severe enough to warrant major treatment.

Available by prescription since only last fall, 13-*cis*-retinoic acid is presently reserved in acne patients for those suffering from severe forms of the illness.

One reason is that mild forms respond well to less rigorous and less expensive care ranging from the use of broad-spectrum antibiotics such as tetracycline and erythromycin to a number of over-the-counter preparations containing benzoyl peroxide.

A second reason is that the retinoid class of drugs may harm a fetus. Therefore, the 13-*cis*-retinoic acid cannot be

Robert Wolpe was deeply self-conscious about his severe acne.

used by a woman patient who either is pregnant or plans to become pregnant while under treatment. Other women patients of child-bearing age must use an effective form of contraception while taking the new medication.

Many myths surround acne. It does not stem, for example, from dirt, certain foods, fatigue, or sexual habits.

Dr. Fitzpatrick said acne follows inheritance of what he called defective "pilosebaceous units." Each such unit under the skin contains a tube (follicle) through which a hair grows. Adjacent sebaceous glands secrete into each follicle an oily substance called sebum.

Acne begins when dead cells, bacteria, and sebum plug the routes to the skin surface. This can produce noninflamed pimples. With the passing of time, these lesions may become inflamed and even turn into pus-filled pimples (whiteheads).

As more material accumulates, the ducts become increasingly swollen and their walls may rupture, spilling irritating contents into the skin.

A break in the deep layer of the skin, the dermis, often produces a cyst, a sac containing fluid or semi-solid matter. The inflammation eventually subsides, but if it was severe, scarring could result.

Sex hormones, particularly the male hormone testosterone, greatly increase the activity of the sebaceous glands.

The clearing after 16 weeks of treatment gave Mr. Wolpe a new outlook.

Lamellar ichthyosis, a disease marked by a buildup of thick layers of skin, responded well to 13-cis-retinoic acid in an MGH study.

"Synthetic oral vitamin A preparations were really the breakthrough."

This explains why acne most often erupts soon after puberty, and probably why males generally suffer the most severe attacks.

Dr. Fitzpatrick said that when he started out in dermatology 35 years ago the principal treatment for acne involved topical sulfur preparations.

"For severely afflicted patients, doctors resorted to what were then regarded as the safe limits of X rays," he said. "While almost always effective, they nevertheless often left the skin permanently damaged, and today some of those same patients are developing skin or thyroid cancers."

When antibiotics came along, the value of tetracycline and erythromycin against acne became quickly apparent, while penicillin offered no benefits. Among externally applied (topical) drugs, benzoyl peroxide has been the most effective acne fighter since the late 1950s or early 60s.

It was during that period that birth control pills first became available. Their ingredients included estrogen, a female hormone which could counteract the overactivity of the sebaceous glands. However, the level of estrogen used tended to cause blood clotting in females, so the amount of hormone was subsequently lowered. Safer and still contraceptive, the new dosage no longer is sufficient to work against acne.

During the past decade, acne researchers assessed topical vitamin A, but it proved to be very irritating and difficult to control.

"Synthetic oral vitamin A preparations were really the breakthrough," said Dr. Fitzpatrick, who also is Wigglesworth Professor of Dermatology and Chairman of the Department of Dermatology at Harvard Medical School.

Ironically, studies of vitamin A derivatives initiated by Hoffmann-LaRoche of Basel, Switzerland, and then by Dr. Peck at N.I.H. were aimed not at finding a cure for acne but at developing an agent to treat cancer. The vitamin has a capacity for making cells mature, just the opposite of cancer's effect on cells.

At N.I.H., Dr. Peck used 13-*cis*-retinoic acid to treat 11 patients for basal-cell carcinomas caused by excessive sunlight exposure or X-ray treatment of acne. He later reported that 16 percent of the cancers disappeared.

At the MGH, Dr. Howard P. Baden directed a study to determine whether

(Concluded on Page 4)

Photographs: Page 1, courtesy of Dr. Thomas Fitzpatrick; pp. 2, 3 (lower), courtesy of Dr. Rhonda Rand; p. 3 (upper), courtesy of Dr. Howard Baden; pp. 4, 7, 8, Myron Daniels; p. 5, courtesy of Dr. Martin Hirsch.

Drawing: Page 6, reproduced with permission of the National Heart, Lung, and Blood Institute.

Certain Blood Defects Can Indicate AIDS

Dr. Robert Schooley briefs technicians in the MGH Bacteriology Laboratories on the AID syndrome.

(Continued from Page 1)

a suppressive effect by a mouse CMV on the immune system of mice.

Human CMV is a major cause of malformations in the fetus, pneumonia and infections in transplant recipients, and contraction of a blood disorder similar to infectious mononucleosis.

Dr. Hirsch said that "the same abnormalities that we found in patients with mononucleosis caused by this virus are now being seen in AIDS patients."

In CMV-induced "mono," patients usually recover after a few weeks, whereas AIDS victims do not overcome the immune abnormalities.

The common thread leading to an AIDS diagnosis is that the tumors and infections which ensue are all characteristic of people with disordered cell-mediated immunity.

"Similar illnesses occur in individuals with defects of T-lymphocytes [a type of white blood cell]," said Dr. Hirsch. "Patients on high doses of immunosuppressive drugs to prevent rejection of organ transplants, for example, have this disordered immunity.

"When we see a tumor or infection where it really ought not to appear, we suspect AIDS. If ensuing T-cell function studies prove abnormal without any known reason, our confidence in the diagnosis of AIDS increases."

Dr. Robert Schooley of the Infectious Disease Unit works with Dr. Hirsch in studying patients with T-cell deficits and the role that CMV and other viruses may play in the affliction.

In a related investigation, Dr. Robert H. Rubin, also of the Infectious Disease Unit, is concentrating on subpopulations of T-lymphocytes. He is looking for abnormalities which may prove invaluable as markers in AIDS patients and offer clues to the disease process.

Since 1981 when AIDS was first diagnosed in this country, pneumocystis carinii pneumonia (PCP) and Kaposi's sarcoma (KS) have led the list of ill-

Acne

(Concluded from Page 3)

13-*cis*-retinoic acid had any value in treating lamellar ichthyosis, an inherited disease which leads to tremendously thick layers of skin. Skin cells pile upon each other in clumps.

The study demonstrated that the drug could cause the cell layers to slough off, leaving the patient with smooth, healthy skin. Improvement was seen in close to 100 percent of the patients treated.

Investigation of ichthyosis and other disorders provided a broad knowledge of the vitamin A derivative so that by the time the acne research began scientists were familiar with the drug's toxicity levels and its side effects.

Dr. Baden, Director of the MGH Tumor Clinic and Professor of Dermatology at Harvard Medical School, said the drug may prove to be the medication of choice to treat patients suffering from multiple skin tumors. Alternative treatment — surgical removal — could then be reserved for unresponsive lesions. ■

Home Care for the Acne Patient

Proper washing is a keystone in the battle against acne.

Regular use of an abrasive soap and a cleaning sponge can not only prevent dead skin, surface oils, and dirt from blocking pores but can also loosen existing plugs of these materials in swollen hair follicles.

Such treatment once a day usually suffices. Allowing the skin to remain moderately dry at other times helps to counter the acne lesions.

For patients with very oily skin, numerous gels and lotions contribute to the desired drying effect.

For some people, frequent sunbathing may improve an acne condition. When natural sunlight is unavailable, a commercial reflector-type sunlamp may be an adequate substitute.

Sunbathing using natural or artificial light demands certain precautions. The eyes must be protected from the light rays, and a health professional should be consulted on the timing of planned treatments.

Acne patients seeking the benefits of the sun should avoid combing the hair over sores on the forehead and cheeks. Such combing not only blocks the sun but also leaves an oily film on the skin.

For the same reasons, patients should be cautious in their selection of cosmetics, avoiding especially the oily "pancake" types of makeup.

Finally, simple external pressure on acne-prone skin can produce lesions. Therefore, while poring over a book or otherwise engaged in concentration, avoid leaning the face on the hands. ■

nesses which have befallen sufferers of the syndrome, the majority ranging in age between 25 and 45.

Pneumocystis is a common organism that usually does not cause pneumonia in healthy people but can cause severe disease in the immunodeficient or immunosuppressed. KS, a form of skin cancer, used to be seen almost exclusively in people over 60 years old outside the United States. Even without treatment, these patients tended to survive eight or nine years after diagnosis.

AIDS has caused a drastic turnabout. All of the pneumocystis pneumonia and Kaposi's sarcoma patients in the AIDS group who were followed for two years or more have died.

"This is not an epidemic in the sense that we think of past epidemics of influenza, measles, or polio," said Dr. Hirsch, "but the numbers of patients have continued to increase since discovery of the syndrome."

. . . the majority of AIDS patients come from only a few sections of the United States.

In addition to identifying the various populations most susceptible to AIDS, investigators have found that the majority of AIDS patients come from only a few sections of the United States.

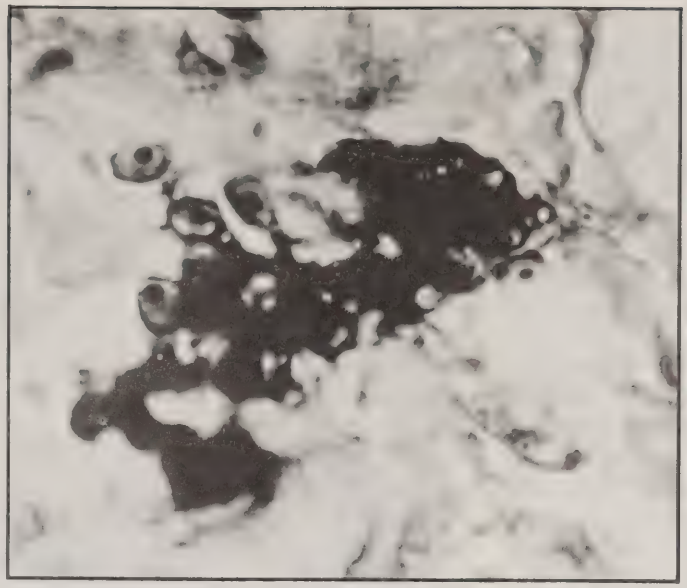
More than half of the patients reside in the Greater New York City area. Another 20 percent live in California, the largest groups in Los Angeles and San Francisco. Most states have recorded at least one AIDS patient.

Addressing a seminar for technicians in the MGH Bacteriology Laboratories, Dr. Schooley described one of the principal roadblocks in the effort to curb AIDS.

"The incubation period [the time that elapses before the first signs or symptoms appear] may be as long as a year," he said.

Haiti was a popular vacation spot for members of New York City's gay community. Fifteen of the first AIDS patients diagnosed in New York had made recent trips to Haiti. Three of five patients reported in Switzerland also had recently completed visits to the island. Half of the AIDS sufferers in Canada were newly arrived Haitians.

Three task forces — two from the federal Centers for Disease Control in Atlanta and one from the University of Miami — went to Haiti to try to determine the incidence of the syndrome there. Inadequate medical record keeping in the country stymied the efforts, but the studies did indicate that AIDS existed in Haiti as far back as 1979 and probably earlier.



Microscopic view of lung tissue affected by a type of pneumonia which commonly follows AIDS

First suspicion that AIDS might be a blood-borne disease came with hemophiliac involvement. Such patients routinely receive a blood-clotting substance derived from the blood of many donors.

AIDS also turned up in individuals who had blood transfusions during surgery. Dr. Schooley told of a 41-year-old Connecticut woman who received two units of blood during a hysterectomy and a year later died of pneumocystis pneumonia. One of the blood donors turned out to have one of the immunologic abnormalities found in AIDS patients.

Kaposi's sarcoma, a skin cancer the incidence of which has risen and spread because of AIDS

In San Francisco, a baby required 19 pints of blood at the time of birth, was healthy for about a year, then developed typical AIDS abnormalities, and died. An investigation revealed that one of the blood donors was a male homosexual who contracted PCP nine months after the baby's birth and also died.

During the past year, MGH doctors have treated between 5 and 10 AIDS patients. Several had multiple afflictions. The diseases treated included PCP, KS, brain cancer, tuberculosis, and CMV.

Even before AIDS was first recognized, studies of Kaposi's sarcoma in areas of Africa, where a high incidence of the cancer prevailed, indicated an association between Kaposi's and cytomegalovirus.

Dr. Hirsch, who is also Associate Professor of Medicine at Harvard Medical School, finds something of a parallel between the history of hepatitis-B and efforts to control AIDS.

"No one thought much about hepatitis-B until the incidence shot up as a result of blood transfusions and the use by drug addicts of contaminated needles," he said. "Then when tests for an antigen [a unique characteristic on a cell surface] became available to screen blood donors for hepatitis-B, the incidence of the disease dropped markedly.

"Our hope is that AIDS will follow the same pattern, that some antigen will be identified that characterizes who carries the causative agent. By identifying the carrier, we hope we will be able to check further spread of the syndrome." ■

The Intricacy of a Simple Breath

The average American enjoys a life span ranging well into the 70s, but by the time he reaches 17, his lungs have already passed their prime.

Documented evidence shows that the lungs begin to lose some of their functioning units during the mid-teens. No amount of subsequent training can restore the lost function.

What then enables the lungs to serve well throughout life? Unless disease intervenes, tremendous adaptability and reserve power.

An adult's lungs contain more than 300 million air sacs. If the walls of these sacs were laid out flat and alongside each other, they would blanket an area the size of a tennis court!

So well endowed are the lungs that the limits of strenuous exertion usually result from factors other than lung exhaustion.

"We've tested a number of Olympic-level athletes," said Dr. Charles A. Hales, Director of the Clinical and Research Laboratories in the MGH Pulmonary Unit. "What fails them is not the ability of their lungs to transport oxygen and carbon dioxide. The athletes generally reach maximum stress because they cannot drive the heart any harder.

"As a consequence, although oxygen levels in the lungs may be normal, the number of vehicles [red blood cells] driven by the heart to truck out the oxygen may not be sufficient to support the amount of work the body's muscles are handling."

Contrary to popular notion, no one ever becomes "breathless." The average human breathes close to 15 million quarts of air a year. Regardless of how much energy is expended, the lungs never relinquish all of their oxygen.

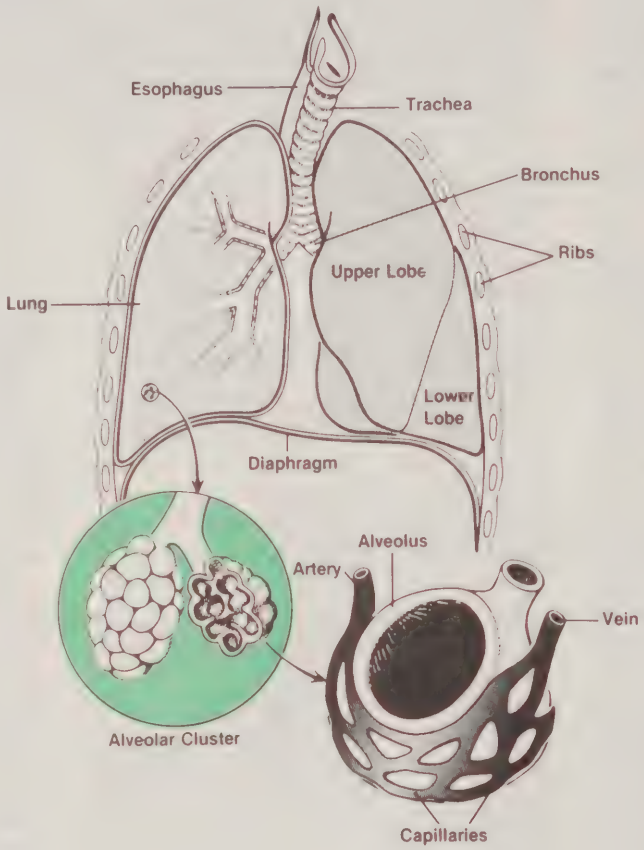
Respiratory centers in the brain control operation of the lungs through nerve impulses directed to the chest wall and the diaphragm, the muscular partition separating the cavities of the chest and the abdomen.

To fill the lungs with air, the diaphragm contracts, and the chest wall moves outward, creating a negative pressure in the chest cavity. Air automatically rushes in to fill the negative pressure space.

Exhaling involves relaxation of the diaphragm and contraction of the chest. The lungs thus dispose of carbon dioxide, a waste product obtained by the air sacs from the blood in exchange for oxygen.

As a person's energy demands increase, such as during running or while climbing a steep flight of stairs, the breathing becomes more rapid to accelerate the gas exchange between blood and air in the lungs.

To reach the all-important air sacs, the air we breathe must travel down the windpipe (trachea) to passageways called



bronchial tubes which connect with each of the body's two lungs. Within each lung the bronchial tube divides into many, many smaller bronchi, including microscopic tubes called bronchioles. They are referred to collectively as the "bronchial tree."

Clusters of air sacs, called alveoli, attach to the ends of the bronchioles and are surrounded by tiny blood vessels (capillaries). The oxygen-carbon dioxide exchange takes place through interaction between the air in the alveoli and the blood in the capillaries.

Some 100,000 people die from lung cancer annually. Smoking is usually the villain.

In examining a patient's lungs, a physician first observes how the person breathes. Does the chest, for instance, rise and fall in a symmetrical manner? A nervous or excited patient tends to have a pronounced chest movement, while a rhythmic in-and-out movement of the abdomen would indicate a relaxed state.

Then, to detect any unusual chest sounds, the doctor taps the patient's chest and also listens with a stethoscope to the breathing. A hollow sound would reflect the normal presence of air. Various more solid noises could signal specific disorders such as pneumonia or asthma.

Sometimes, knowing how much air a patient can breathe in and out helps a physician to assess lung health. A simple, portable device called a spirometer can provide this data. The patient breathes into a tube, and a stylus records on a revolving drum the amount of air being transported.

One of the most common tools used in diagnosing a lung problem is still the familiar chest X ray. But a normal chest X ray does not exclude lung disease. A more sophisticated CT (computed tomography) scan would provide even greater information on lung structure.

And techniques are available to see the lungs working.

"We can put a bronchoscope right down into the breathing system and get a direct look at the breathing tubes," said Dr. Hales.

"Also, we can give the patient a radioactive gas [xenon], place him under a nuclear [gamma] camera, and by looking at a screen follow the action of his lungs."

To protect the normally light and airy lungs, each about the size of a football, hairlike structures called cilia line each bronchial tube leading to the alveoli. By beating rhythmically and in unison back and forth some 900 times a minute, the cilia whip out most solid contaminants that may threaten the

To assess a patient's lung function, Pulmonary Laboratory Supervisor Jean Sullivan uses a blood gas analyzer to measure oxygen and carbon dioxide in blood drawn from an artery of the patient.

lungs.

Certain white blood cells called macrophages (*MGH News,* November 1982) also protect the lungs by gobbling up microorganisms and foreign particles and dissolving them with digestive enzymes.

"There is a risk here, however," said Dr. Hales. "The macrophages might not be able to consume some organisms. The enzymes might spill out, instead, and begin to digest the lung itself."

The doctor said this may be a contributing factor in the development of emphysema, a disease which destroys the elasticity of the lungs and therefore their ability to function (*MGH News,* January–February 1982).

Emphysema is 19 times more common among people who smoke cigarettes than among nonsmokers, and many more macrophages can be found in the lungs of smokers than nonsmokers.

"You may not notice this unless you have already done something to compromise the function of the lungs, such as to inhale smoke or some other irritant," said Dr. Hales. "The incidence of pneumonia or bronchitis [an inflammation of the bronchial tubes] appears to be much higher, for example, among people who smoke. The illnesses could be complications of a cold or the flu."

Lung cancer, an uncontrolled growth of abnormal cells, constitutes the deadliest disease affecting the lungs. Some 100,000 people die from lung cancer annually. Again, smoking is usually the villain.

Dr. Hales, who is also Associate Professor of Medicine at Harvard Medical School, said the treatment for most forms of lung cancer is still removal of part or all of the organ.

One type of cancer called oat cell carcinoma does respond to drugs. "They make possible a two-year chance of survival," Dr. Hales said. "While not a very long time, it's better than the three to six months which used to be the prognosis."

The pulmonary specialist believes that some of the most impressive successes in his field will involve immunology.

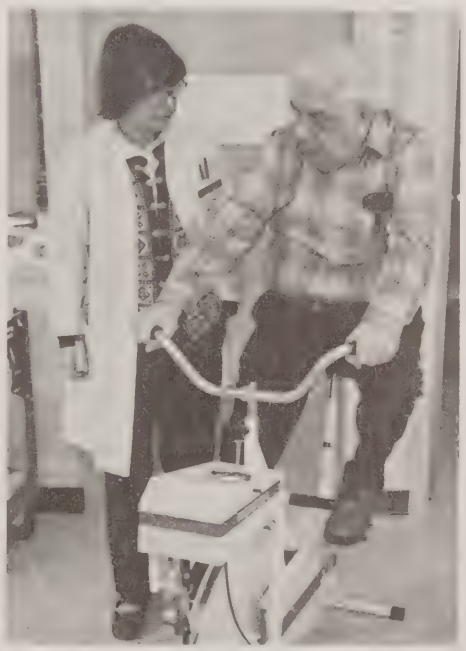
With the availability of cyclosporin, a drug with a remarkable ability to prevent rejection of substitute organs, Dr. Hales envisions more lung transplantations in such circumstances as lung injury from an accident or on-the-job exposure to substances devastating to the lungs.

The doctor also said investigators are beginning to understand a number of scarring processes that take place in the lungs.

In the operation of the body's immune, or germ-fighting, system, white cells called lymphocytes are described as the "brains" behind the body's soldiers, the macrophages. Apparently, in actions between the lymphocytes and macrophages, skin cells (fibroblasts) are activated to form the scarring.

"Once we really learn how the lymphocytes and macrophages talk to each other," said Dr. Hales, "we may be able to produce a drug that will interrupt the conversation when the fibroblasts enter the picture." ■

In a newly launched MGH pulmonary rehabilitation program, Chest Physical Therapist Rosanna Piccolomo pats the back of Mary A. Kelley to dislodge mucus in her lungs.



With Chest Physical Therapist Terry Michel supervising, John Watson, a pulmonary patient, pedals an exercise cycle to condition his body muscles.

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

If Turtles Could Only Speak

Without oxygen support, most human beings would have to struggle to remain under water for more than a minute and a half.

Highly trained professional divers might stretch this to three minutes but rarely much longer.

All of which heightens respect for the lowly turtle.

Seemingly lazy and unable to get around very fast, these air-breathing creatures nevertheless can remain submerged for up to six months!

Bernard Hitzig, Ph.D., a physiologist in the MGH Pulmonary Unit, is studying the remarkable underwater ability of these reptiles and whether the unique mechanisms involved can be applied to human life.

"Simply knowing how turtles are equipped to deal with lack of oxygen may help us to better understand how to cope with abnormal states marked by oxygen deficiency," he said.

"Turtles must be doing something very right. They're the only living descendants of the so-called stem reptiles which gave rise to modern mammals and have been around, essentially unchanged, for some 220-million years."

Cold-blooded creatures whose body temperature varies with their environment, turtles live up to 200 years.

Dr. Hitzig's research centers on red-eared, fresh-water turtles, the same species as those baby turtles that children once bought as pets.

The laboratory specimens, however, are about 10 years old, have a shell a foot long, and weigh between five and six pounds.

Their lungs are enormous. Extending from one end of the shell to the other, the lungs can store enough air to last an hour or more.

A so-called diving reflex helps the turtles to make best use of the available oxygen. The reflex alters distribution of blood flow, giving higher priority to the brain and heart. The body's utilization of energy (metabolic rate) drops drastically, slowing the heart and consequently lessening its need for oxygen.

Humans also enjoy a diving reflex, but it operates much less efficiently than that of the turtle. One reason is that unlike humans with their four-chambered heart, the turtle has a three-chambered heart (one less ventricle, or pumping chamber). This facilitates blood circulation to vital areas and bypasses the lungs when the air supply runs out.

"It was once thought that a three-chambered heart is inferior to a four and that the human heart represents a step up on the evolutionary scale," Dr. Hitzig said. "This is not true. The three-chambered heart is absolutely essential for the turtle's survival in the circumstances under which it lives."

How do turtles manage to survive after depletion of their oxygen supply?

"Their brain has a remarkable capacity to switch to a form of energy production which does not rely on oxygen," said Dr. Hitzig, who is also Assistant Professor of Medicine and Physiology at Harvard Medical School.

"This so-called anaerobic [without oxygen] metabolism produces a compound, adenosine triphosphate, which supplies energy to all body cells. To a very limited extent, young children, particularly newborns, also have this unusual production capability."

The mechanisms of anaerobic metabolism help to regulate the delicate balance between acidity and alkalinity in the brain. "By changing the ionic composition [i.e. sodium, potassium, etc.] in the brain's extracellular fluids," the MGH physiologist said, "we may be able to help people cope with critical stages of such conditions as respiratory distress or marginal perfusion of the brain.

"For example, if a person fell through ice into frigid water and lacked an artificial oxygen supply, the mechanisms that turtles use perhaps could be applied to try to save that individual's life after rescue from the water."

One of the basic findings in the studies conducted by Dr. Hitzig and a colleague, Dr. Meinhard Kneussl, a Visiting Fellow from Vienna, is that in a number of respects humans and turtles are much more similar than different. ■

Although air breathers, these turtles can adapt to living under water for up to six months.

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 42 No. 3 April, 1983

Studies of Plant Growth May Improve Human Life

Getting at the Source of Pain

Someone once said: "If flames broke out on Forty-second Street, you wouldn't put out the fire by dumping water on all of Manhattan."

This simple logic helps to explain why a new method of administering morphine to quell intractable cancer pain is winning ever increasing medical acceptance.

Given system-wide, the narcotic dose required for the relief of severe cancer discomfort often leaves the patient groggy and inactive. But what if morphine, long a proven pain reliever, were given at a specific point near the actual source of the pain?

In the past three years, this idea, carried out first in laboratory and later in human studies at the MGH, has gone far toward a long-term alleviation of pain from various cancers without depressing the patient's cognitive, sensory, or motor function.

The concept of "putting the hose right on the fire" arose when investigators showed that morphine acted not only in the head but also to a large extent in the spinal cord. Actually, the cord was found to contain a high concentration of receptors for pain killers like morphine.

Pelvic cancers, such as ovarian, rectal, or bladder tumors, may encroach upon nerves coursing from the lower part of the spine through the pelvis to the genitals, legs, etc. The pain can be excruciating.

To treat such distress, two MGH doctors, Charles E. Poletti, a neurosurgeon, and Donald P. Todd, an anesthesiologist, designed two systems which enable patients themselves to deliver morphine when needed directly to the lower spine.

Each device implanted in the body contains a tube (catheter) to carry the drug to the dura, the outermost membrane covering the spinal cord. The morphine is then absorbed through the dura into the cord.

One delivery system features an indwelling reservoir which can hold a four-month supply of morphine. The patient controls the dosage through finger pressure upon a combination valve and pump implanted just under the skin surface.

In the other system, one end of the catheter protrudes from the skin.

(Continued on Page 4)

Greenhouse manager Marilyn Brown tends tobacco plants used in genetic research.

As night fell and personnel headed home from laboratories and offices in the Edwards Memorial Research Building, a glow atop the seven-story MGH structure pierced the darkness.

The day was far from over in the new greenhouse operated by the hospital's Department of Molecular Biology.

Regardless of the season, the standing order calls for 16 hours of light every day in the glass-enclosed structure. Powerful, high-pressure sodium lamps rigged to timers replicate daylight.

An elaborate climate control system also purifies air by passing it through charcoal filters and closely regulates the temperature and humidity in the 1,300-square foot workplace.

Everything possible is being done to provide optimal conditions for the growth of specially selected plants with the hope of learning more about their genetic makeup and, in particular, how these inherent characteristics might be altered or improved.

"The knowledge gained from studying the basic biology of plants may one day have a direct impact on human nutrition by paving the way for better crop production," said Howard M. Goodman, Ph.D., Chief of the Molecular Biology Department.

He also pointed out that what is learned "may give us new insights into normal and abnormal processes in animal [including human] cells."

When it comes to growth, he explained, plants and animals have much in common at the molecular level.

"The respective genes look very similar," he said, "and so far as we know the language of the genetic code [the system by which genetic information is passed on to protein-making machinery]

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114 Telephone (617) 726-2206

Martin S. Bander	*Editor*
Myron H. Daniels	*Assistant Editor*
Doris G. Schreckengaust	*Copyreader*

EDITORIAL BOARD

J. Robert Buchanan, MD	*General Director*
Kurt J. Isselbacher, MD	*Research, Medicine*
Paul S. Russell, MD	*Surgery*
Ronald A. Malt, MD	*Surgery*
Roger H. Sweet, MD	*Utilization*
Stanley Bennett	*Photography*
Robert J. Galla	*Designer*

EDITORIAL:

A One-Sided Approach to Hospital Costs

External attempts to control the rate of inflation in hospitals have typically set limits on increases hospitals charge patients. But the controls customarily fail to restrict how much the outside vendors charge hospitals for goods and services. That principle certainly holds true for Chapter 372, the Massachusetts cost control law that became effective last October 1. This is one of the law's aspects that places hospitals in between a landslide and an erupting volcano. Under Chapter 372, a hospital can only increase charges to patients by a small percentage each year. That limit becomes quite difficult to observe if businesses raise charges for goods and services to hospitals by, say, two to three times as much every year.

The *News* sampled several pieces of equipment needed to run an inpatient facility. The comparison years were selected by the manufacturers themselves because the figures were readily available. For an operating room table, a standard manually operated version that cost $1,813 in 1949, we now pay $12,700, a 700 percent increase or an average of 21 percent every year. An 80-inch stretcher that cost $742 in 1969 now costs $1,997, a 269 percent rise. That averages 21 percent annually. A large sterilizer that cost $4,170 in 1949 has soared to $41,600, an increase of 998 percent that averages 30 percent a year. An EKG heart monitor that cost $850 in 1965 now costs $2,870, an increase of 338 percent or a 20 percent annual average rise. And an electric bed with accessories that cost $620 in 1970 costs $1,430 13 years later, a rise of 230 percent. That is an average of 17.7 percent annually. Since 1972 the cost of a carton of standard-sized X-ray film has increased from $413.19 to $1,126.85, a leap of 273 percent or 27 percent a year. Some of these products like the sterilizer and the EKG embody significant technological improvements. On the other hand other supplies like the operating room table, the X-ray film, and the stretcher have changed very little technologically, if at all, each year.

Often major technological improvements result in significant advances in diagnosis and treatment. In these instances — and they are frequent — the changes translate to better health for the patient. Another less common matter are those products lacking technological improvements and which become more expensive for hospitals to buy. The hospital has no choice but to purchase these devices. With their high rate of annual inflation, though, they tax the cost-cutting capability of even the most efficient administrator. The law that dictates rigid controls for hospitals but not their suppliers has to be judged as assailable at best. Let us hope that members of the Business Roundtable will take a long look at themselves and remember a quote often used by a former MGH General Director, Dr. John Knowles: "We have met the enemy, and they are us."

A Plant Can Regrow From Only One Cell

(Continued from Page 1)

is the same in both plants and animals."

Despite these similarities, plants do exhibit unique capabilities. In certain circumstances, for example, it is possible to obtain a single cell from, say, a plant leaf and, using special culture techniques, regrow an entire new plant from the one cell.

"That's the equivalent of taking a little piece of human skin, breaking it apart to get a single cell, and then, with the cell, creating an identical human," Dr. Goodman said.

Plant regrowth from the smallest structural unit of an organism creates a remarkable technical tool with which to undertake a variety of far-reaching experiments.

Dr. Goodman's research is a continuation of work which the renowned scientist conducted at the University of California, San Francisco, before he came to the MGH to fill his present position and also to accept appointment as Professor of Genetics at Harvard Medical School.

He is a pioneer in the development of techniques involving DNA (deoxyribonucleic acid), one of nature's basic building blocks, and the application of these methods to the structure and function of genes.

His appointment at the MGH climaxed a several-year worldwide search for someone to begin a new department in basic genetic research.

Dr. Goodman and his colleagues are presently concentrating on how to isolate particularly desirable plant genes and add them to a cell of another plant with the hope of producing an improved variety.

Through such a process, a food plant susceptible to drought might be made more drought resistant. Instead of having to be sprayed with chemical insecticides, a plant might be given a natural means of warding off insects.

Dr. Goodman emphasized the basic research nature of his team's work. "While these ideas may seem possible in principle," he said, "putting them into practice can be a real challenge."

First of all, one must find a way of identifying those plant cells which

Photographs: Pages 1, 3, 4, 5, 6, Myron Daniels; p. 8, courtesy of Dr. Richard R. Liberthson

Drawings: Page 4, courtesy of Dr. Charles E. Poletti; p. 7, MGH Medical Art Department

carry specific, desired information. Then, it might take a study of a million plant cells to locate a hundred or so appropriate ones.

The researchers also are trying to learn what differentiates tissues or organs of a plant. More specifically, what makes a root a root . . . a stem a stem . . . a leaf a leaf.

By knowing what genes are expressed to make various components of a plant, one has the potential to more easily effect and control desired alterations in its structure.

Tobacco plants are used most often for this work because 90 percent of the time a cell taken from one of these plants will produce a healthy, rapid growing new plant.

Frederick M. Ausubel, Ph.D., an MGH molecular biologist, uses the greenhouse to conduct extensive studies on nitrogen, essential to the making of amino acids, the chief components of proteins.

Normally, bacteria break down nitrogen compounds left in soil by other plants or by animals. This nitrogen, in the form of nitrates, is then taken up by plants and used to manufacture important products such as proteins and nucleic acids (DNA). Often, however, to assure growth of important food crops, farmers must add large amounts of costly nitrogen-rich fertilizers.

Ironically, 80 percent of the earth's atmosphere consists of nitrogen gas. To become usable by plants or animals, the gas must first be converted into ammonia. Only certain bacteria can achieve that transformation.

The world's major food plants — corn, wheat, and rice — do not have the bacteria necessary to carry out this nitrogen fixation process. But a plant family called legumes, comprising peas, beans, clover, and alfalfa, does.

Elaborate lighting and climate control measures assure ideal conditions for the growth of plants specially chosen for study.

Using alfalfa plants in the greenhouse because they are the most convenient legume to work with, Dr. Ausubel is striving to expand man's knowledge of how such plants and their bacteria interact to allow use of atmospheric nitrogen.

"If one could transfer such bacteria to other plants and establish this same symbiotic [cooperative] relationship," Dr. Ausubel said, "one could eliminate the need for a lot of fertilizer. This would have a tremendous impact on the agricultural economy."

In one experiment, tiny alfalfa plants are being grown in test tubes containing a gel-like nutrient. To avoid contamination, the opening of each test tube is covered, but nitrogen and carbon dioxide in the air can still enter.

"We're testing individual bacteria on separate plants, hoping to identify genes which have become mutated or altered and fail to function in the nitrogen fixing process," Dr. Ausubel declared. "By learning what goes wrong, we can deduce what happens when things go right."

The MGH scientist, who is also Professor of Genetics at Harvard Medical School, described a second experiment which is aimed at studying alfalfa plant roots.

He said these plants are cultivated under a system called aeroponics. They grow on a screen covering a water-filled box. The screening allows the developing roots to dangle over the surface of the water. A fan stirring the water creates a mist which feeds the root systems. The aeroponics method assures that the roots will be free of impurities.

"At the proper time," Dr. Ausubel said, "we take the roots and extract the

(Concluded on Page 4)

Getting Direct Help to Relieve Pain

(Continued from Page 1)

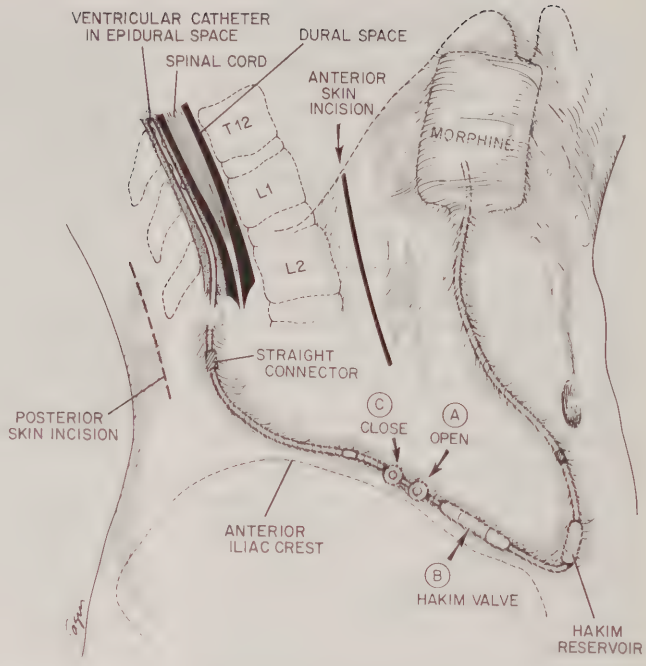
When in pain, the patient can simply cleanse the rubber diaphragm on the catheter with an alcohol compress and inject the amount of morphine the doctor has prescribed.

Reporting in the *Journal of Neurosurgery* on use of these systems in patient care, an MGH team, including Drs. Poletti and Todd, wrote:

"It is clear that direct spinal administration of morphine offers a new and promising dimension to the therapeutic efficacy of opiates, eliminating the need for chronic systemic narcotic treatment for many types of cancer pain."

Even as this report was being drafted, a third implantable system became available to deliver morphine to pain sites. Codeveloped by Dr. Perry J. Blackshear, now of the MGH, and a University of Minnesota team, the method features a Freon-driven pump which continuously infuses the morphine into the epidural space from a reservoir containing a two- to four-week supply.

The United States Food and Drug Administration last month approved use of this system for morphine application. Trials are under way to assess the pump's value in delivering other drugs, such as insulin for diabetics.



Sketch shows a completely implanted system for delivering morphine from a reservoir to a painful spinal site. The patient administers the drug himself by pressing through the skin upon a valve..

The various devices underscore rapid strides made in recent years to learn more about the cause and prevention of pain. The improved understanding has resulted in the establishment of several pain units or clinics at the MGH.

The various facilities involve specialties such as neurology, neurosurgery, oral surgery, oncology (tumor study), anesthesiology, and psychiatry.

Although established as separate entities because of the particular medical interests of the participants, the clinics interact to assure the most thorough patient care.

"Each clinic anticipates visits by patients whose problems have proved dif-

Greenhouse

(Continued from Page 3)

proteins and nucleic acids made specifically by interaction of the plants and the bacteria living in the roots. We hope our study of these substances will help us to understand what special proteins and special genes are being utilized for this process."

Although plants are much simpler than animals, Dr. Ausubel said the study of how bacteria interact with plants might prove to be a good model for ultimately understanding more complex relationships between disease-causing bacteria and people.

The MGH greenhouse, opened only a few months ago, soon will have a sister. The second greenhouse will occupy close to 2,000 square feet of space atop the Wellman Research Building, presently under construction adjacent to the Edwards Memorial Research Building.

Both greenhouses were constructed using funds from a grant from Hoechst AG of Frankfurt, Germany, a leading international chemical company. The company has also provided over $10.8 million for the construction and finishing of the upper four floors of the Wellman Building. This space will be the permanent home of the Department of Molecular Biology.

By studying plants growing in test tubes, researchers hope to identify genes which fail to promote use of atmospheric nitrogen.

The funding for the new research structure includes $15 million donated by Arthur O. and Gullan M. Wellman after whom the building is named.

In addition to providing more laboratory space for Dr. Goodman's department, the second greenhouse will permit an expansion of experiments that could lead to new and earlier results.

Hoechst AG also underwrites the costs of Dr. Goodman's MGH department. Terms of a 10-year, $50-million plus agreement provide that Hoechst will be entitled to a license under any patent that results from research sponsored by the company. The MGH retains rights to the patent.

MGH investigators will choose their own research projects, are open to collaboration with others, will write their own scientific articles, select the journals for publication and meetings for presentation, and decide when to submit articles to journals.

Since the new department's work is basic, it will be up to Hoechst to seek in its own laboratories the practical applications for any advances that come from the work. *Plant studies represent only one segment of the overall investigations of the Department of Molecular Biology which has a broad-based program aimed at understanding, at the molecular level, various aspects of life processes.* ■

ficult to diagnose," said Dr. Poletti. "In the past, patients all too often had to consult one specialist after another at considerable expense to find relief from persistent pain.

"It is therefore of enormous benefit, both for the doctors and the patients, to maintain lines of interdisciplinary communication and cooperation."

In the Facial Pain Clinic directed by Dr. R. Bruce Donoff, MGH Acting Chief of Oral and Maxillofacial Surgery, between 10 and 15 percent of patients turn out to have an identifiable physical disorder, such as a sinus abnormality, bone tumor, or inflamed nerve affecting facial sensation (trigeminal neuralgia) (*MGH News,* October 1981).

Dr. Poletti frequently collaborates with Dr. Donoff and another oral surgeon, Dr. David A. Keith, in treating facial pain patients. When no physical evidence can be found to account for discomfort, the assistance of Dr. Anthony J. Bouckoms, an MGH psychiatrist, is especially valuable.

"With his special training he can determine if a patient has deeply rooted psychological problems," said Dr. Donoff.

Dr. Bouckoms said most patients in the pain clinics have a significant psychological overlay. "Even in cancer patients," he said, "the distress is 50 percent physical pain and 50 percent anxiety, depression, sleeplessness, nausea, or fear. Even without changing the physical pain, one can often alter the other suffering that the patient feels."

Since the biochemistry of pain and of depression are very similar, Dr. Bouckoms may prescribe antidepressant drugs such as doxepin or trazodone in either situation.

In instances of pain caused by actual nerve damage, carbamazepine (Tegretol) and diphenylhydantoin (Dilantin), both anticonvulsive medications, are frequently helpful.

The vast majority of patients who visit the pain clinics do not need surgery. In addition to giving drug treatment, the clinics often call upon the Anesthesia Pain Unit, directed by Dr. Todd, to perform nerve blocks.

These involve injections of an anesthetic into a painful, injured nerve to make the patient comfortable until the nerve can heal.

"Low-back difficulties account for a large number of patients we see," Dr. Todd said. "Disc problems often lead to an irritation of nerve roots. Cortisone given with the anesthetic helps to speed recovery."

Dr. Todd's group has been able to provide outpatient treatment on a regular basis since November when they moved into a new area that is a part of the MGH Ambulatory Care Center's Surgical Day Care Unit.

Other conservative treatments that the clinics might consider to combat pain include electrical stimulation of a nerve, hypnosis, biofeedback, or physical therapy.

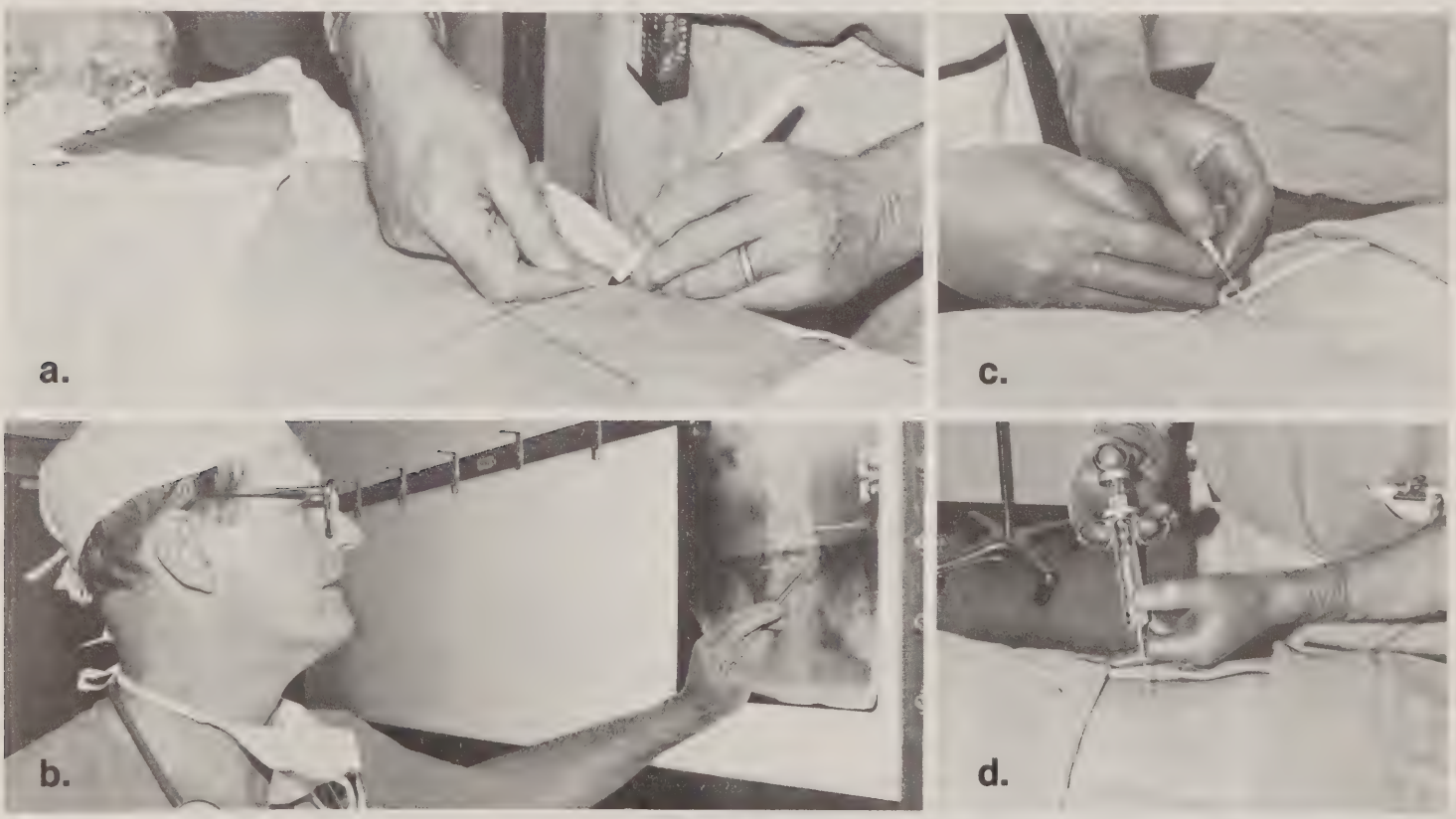
In their effort to relieve discomfort, the Neurological Pain Service under Dr. Raymond J. Maciewicz and Neurosurgical Pain Service directed by Dr. Poletti are continuing an MGH tradition carried on for many years by Dr. James C. White when he was Chief of Neurosurgery and by his successor as Chief, Dr. William H. Sweet.

Dr. Sweet and the late Dr. White provided medicine with a vast body of knowledge on pain, including two textbooks on which they collaborated.

The neurological and neurosurgical pain units strive to eliminate suffering without destroying nerve tissue. Dr. Poletti told of a nurse who developed chronic pain at the back of her head some six years after a diving accident.

"She had every indication of occipital neuralgia, a condition requiring the cutting of one or more nerves," he said, "but on the possibility she might have a pinched nerve, we obtained some special X rays. They revealed an arthritic spur which had not shown up on regu-

(Concluded on Page 6)



To perform a pain-relieving nerve block, Dr. Donald P. Todd first (a) draws a diagram to plot the site of treatment, (b) uses skin-surface needle markers, visible on X ray, to locate skeletal reference points for needle placement, (c) inserts a needle to touch the nerve, and (d) injects an anesthetic to halt the pain, then cortisone to promote healing.

Extensive Research To Counteract Pain

(Concluded from Page 5)

lar X rays. The spur was pressing on two nerves. Just relieving this pressure with a procedure that avoided cutting nerves solved the patient's problem."

When for some reason nerves become cut or damaged, cells in the spinal cord that normally receive input from these nerves begin to fire very rapidly, inflicting pain. A current passed through an electrode inserted into the spinal cord can kill the abnormally firing cells and thus blot out the pain.

Surgeons sometimes turn to this operation when an accident causes the tearing of an arm nerve from the spinal cord (brachial plexus avulsion) or when a patient, following an amputation, is stricken with so-called phantom pain.

Dr. Poletti described cancer patients as one of the largest groups for whom surgery has something to offer to counter pain. He said that the epidural catheter systems, for example, enable patients living many miles from a hospital to treat themselves without undue side effects "and, in our experience, morphine gives very satisfactory results in five out of six cancer patients."

Dr. R. Bruce Donoff investigates a complaint of jaw discomfort in the Facial Pain Clinic.

Initially, these patients often are in such distress that they come to the hospital by ambulance to see various specialists. The Cancer Pain Clinic makes such consultations possible in a single visit.

Drs. Alfred M. Cohen and William C. Wood, cancer surgeons; Dr. Fred H. Hochberg, of Neurology; and Dr. Poletti participate in the clinic's activities.

As treatments are prescribed, the battle to conquer pain also goes on behind the scenes.

Neurosurgery and neurology operate separate but collaborative basic research laboratories to study the influence of inherent pain suppressors in the body's central nervous system.

With a three-year grant from McNeil Laboratories, a pharmaceutical firm, Dr. Beth Hendrickson, a Research Fellow in Neurology, is studying the mechanism of pain in bone.

Another investigation involves patients who suffered strokes affecting the cerebral cortex, the brain's outer layer, which is responsible for man's higher mental functions. Some researchers believe the cortex plays a major role in man's tolerance for chronic pain.

Dr. Donoff of Oral and Maxillofacial Surgery said the drug industry is beginning to make great strides against pain. "The industry," he said, "is honing in on abilities of drugs to suppress or inhibit certain molecules involved in specific sensations, pain being one."

He would not be surprised, he said, if someday patients will be able to undergo major surgery without general anesthesia. "The trends in research are going that way," he declared. ■

Coping with Patient and Family Guilt Feelings

When injury or illness endangers life, medical personnel very often find their roles as health care providers complicated by unexpected factors.

They must stand ready to encounter feelings of guilt in both the patient and his family.

"It is an irrational guilt, so you won't always anticipate it, and, more than that, you may not even recognize it," Rabbi Harold S. Kushner of Natick, Mass., recently told an MGH medical gathering (Pediatric Grand Rounds).

"What it seems to be is a rage for order in our minds where we insist on making sense of what happened when the fact is not everything makes sense."

The patient is very apt to say to himself, "I must have done something wrong, and now I'm being punished for it." At the same time, sorrowing relatives may simply feel guilty of being well while someone they care about and would give their lives for is suffering.

The spiritual leader of Temple Israel in Natick is intimately acquainted with what can pervade the mind as the life of a loved one fades.

In 1977, his son, Aaron, died at the age of 14 from a rare condition known as progeria (premature aging). Subsequently, Rabbi Kushner authored a book, "When Bad Things Happen to Good People." Published by Avon Books, it has become a best seller.

Rabbi Kushner stressed to his MGH audience that both sick people and their kin need a tremendous amount of reassuring, caring, and hand holding.

"They are hurt and angry," he said, "and they have a right to feel that what is happening to them is tragic. We deprive people of this right when we say things like, 'I see a lot of people who are worse off.'"

The sense of guilt that prevails is easily deepened. By not responding on schedule to treatment, for example, the patient may feel that he is letting down the doctor and the nurses.

At the same time, the family, sitting tensely in a waiting room for the longest time to hear of some medical development, may get the impression that they are under foot.

"Both the patients and their loved ones are so terribly vulnerable that we must go out of our way not to seem critical or resentful of them," the rabbi cautioned.

Rabbi Kushner offered a different course: It's so helpful to give the patient and the family a sense of control, of involvement, of decision-making, rather than a sense of passivity and helplessness.

"When our son was very ill," he said, "and had to take 15 pills a day, we would remind Aaron at 1 o'clock that it was time to take some, but he would say, 'I won't. I'll take them at 1:30.' He wanted to feel that he was not simply following someone's directions, but that he had some sort of discretion over what he did."

Rabbi Kushner told his audience that "you won't always be able to save lives" but suggested that medical effectiveness might be more properly measured in terms of whether the inevitable was made more bearable and whether the patient came to the last stage of his life as human as he could be. ■

Planning to Go Abroad? Take Precautions

In this age of jet air travel, few places in the world are far from any American home.

By air from New York City, one can reach Port-au-Prince, Haiti, in 4½ hours; Mexico City, 5½ hours; Buenos Aires, 10½ hours; Bucharest, 11 hours; Nairobi, Kenya, 16 hours; or Singapore, 22¼ hours.

Every year some 10 million Americans go abroad, more than half to bask in sunnier, warmer climates, but many soon find they cannot stomach the new environment.

Regardless of where a person travels, to another highly developed country or to a poor one, the body often must cope with unfamiliar bacteria or other organisms. While native populations may appear immune to the germs found in food or drink, visitors can become quite ill.

"I know a professor in England who used to travel to the United States frequently but then stopped the visits," said Dr. Kurt J. Isselbacher, Chief of the Gastrointestinal Unit at the MGH. "It so happened that every time he came here he developed diarrhea and fever."

Between 25 and 40 percent of Americans who travel abroad suffer from some so-called GI problem, usually a mild ailment that runs its course in a few days. In Mexico, the incidence of illness has reached 50 percent of the approximately three million Americans who visit there annually.

A major cause of traveler's diarrhea in Mexico, as well as a number of other countries, came to light as the result of a medical gathering in Mexico City in the fall of 1974.

Since the Fifth World Congress of Gastroenterology was scheduled there, Dr. Isselbacher, then president of the American Gastroenterological Association, arranged to collect blood and stool samples from delegates and family members before, during, and after their Mexico visit. Investigators would then examine the specimens for any disease-causing agents.

The results, published in the *New England Journal of Medicine* two years later, showed that of 121 study participants, 59 (49 percent) had been stricken with diarrhea. More than a half dozen organisms were involved, but one, *Escherichia coli (E. coli),* figured in 45 percent of the illness incidents.

No one had suspected *E. coli* because it inhabits the human intestinal tract and rarely causes problems.

"What turned up in the investigation, however, were strains of toxin-producing *E. coli* which the visitors to Mexico presumably never had in their intestinal tract previously," Dr. Isselbacher said. "The data suggested that the infection was traced primarily to a consumption of salads containing raw vegetables."

When traveling in a country where visitors commonly develop intestinal upsets, care in choosing food and drink is a must.

Between 25 and 40 percent of Americans who travel abroad suffer from some so-called GI problem.

Hot, cooked foods are generally safest. Avoid: any dish containing raw vegetables, fruit lacking a thick, disposable peel, any unpasteurized dairy product, and cold foods not served cold, such as unrefrigerated desserts.

Hot drinks such as coffee and tea are usually safe, as are canned or bottled beverages. Avoid tap water not properly treated, and be suspicious of ice cubes.

Once it strikes, how can one cope with the ailment often referred to as turista, Montezuma's revenge, Delhi belly, or traveler's diarrhea.

Bismuth subsalicylate (Pepto-Bismol) can relieve symptoms, but the sizable quantity needed for proper care makes the medication inconvenient to carry.

Lomotil, a drug which slows intestinal activity, may be preferable. Some physicians argue, however, that slowing intestinal contractions may delay elimination of the offending organism.

Two antibiotics, doxycycline (a long-acting tetracycline derivative) and a combination of trimethoprim and sulfamethoxazole have proved useful against diarrhea.

Dr. Isselbacher, who is also Mallinckrodt Professor of Medicine at Harvard Medical School, cautioned, however, that doxycycline can make skin hypersensitive to the sun and "a severe sunburn can be just as big a problem as diarrhea."

Although the trimethoprim-sulfamethoxazole combination can also have side effects, including allergic reactions, Dr. Isselbacher regards this medication as relatively safe.

Last fall, the *New England Journal of Medicine* published results of a study of trimethoprim used alone and in combination with sulfamethoxazole. The study involving diarrhea-stricken American students in Mexico showed that the drugs halted the illness in 30 hours. It lingered for 93 hours in others who had taken inactive substances called placebos.

Should prophylactic measures be taken in advance of travel to areas where diarrhea may result? Dr. Isselbacher thinks early protection for older people in delicate health and for infants would be warranted since fluid losses might lead to serious problems for them. *(Concluded on Page 8)*

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Foreign Travel Can Hinge on Health Shots

(Concluded from Page 7)

If an intestinal upset persists longer than four or five days, leads to blood in the stool, or causes a temperature higher than 103°F, medical help should be sought. The illness could be something more serious than traveler's diarrhea.

Travel outside the United States can expose a person to a variety of diseases. Although smallpox has been wiped out worldwide, malaria is on the increase. It remains a major threat in wide regions of Central and South America, Africa, and Asia.

"The number of malarial parasites resistant to the drugs customarily used to ward off or treat malaria is mounting," said Dr. John S. Wolfson, a physician in the MGH Infectious Disease Unit. "The recommendations for antimalarial drugs to take before an individual enters certain areas have changed significantly in the past few years."

Protection against malaria involves taking pills before, during, and after a trip. The quantity and type of medication depend on the region visited.

People who contract malaria may not feel ill from the disease until weeks, months, or, in unusual instances, even years after their travels.

Dr. Wolfson added that anyone planning to visit rural areas of a third-world country should also consider receiving immune globulin for protection against a possible hepatitis A infection.

Dr. Terrence A. O'Malley, Medical Director of the MGH–Logan Airport Medical Station, said some countries still mandate shots for certain diseases before granting admittance to visitors.

Some countries in South America and Africa, for example, insist on inoculation against yellow fever. Lacking such protection, a traveler would be vaccinated upon arrival and quarantined for 10 days to prove he does not have the disease.

The Philippines and most nations in Asia and Africa require shots against cholera, although the risk of tourists getting that disease is very low and cholera vaccines have limited effectiveness.

Vietnam requests that travelers be vaccinated against plague.

The MGH–Logan Airport Medical Station administers vaccines against yellow fever, cholera, plague, tetanus, typhoid, polio, measles, and mumps, gives immune globulin for protection against hepatitis, and will issue prescription drugs against malaria.

Dr. O'Malley advised vacationers to plan their travels many months in advance because some of the vaccinations, such as protection against polio, require a series of shots over an extended period to assure maximum benefit.

"Preventive measures apply to everyone, but people with significant medical problems should not travel unless their condition has been stabilized," he added. "Individuals, for example, who have experienced a heart attack probably should not travel until about six months later, provided their condition permits it."

To guard against motion sickness, people traveling by air often do quite well by taking a sedative or an antinausea drug before departing. At sea, drugs such as meclizine can prevent motion sickness. A dermal patch, placed behind an ear like a Band-Aid, also offers protection. Each patch contains enough skin-penetrating medicine to last 72 hours.

Finally, anyone requiring a prescription medication should carry along an extra supply when going overseas for extended periods. Drugs sold in this country may be marketed abroad under different names and in different dosages, even by the same company. ■

Fruits and vegetables being taken to market by boat on a river in Bangkok, Thailand, easily pick up disease-causing organisms.

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 42 No. 4 May, 1983

Specialists Seek to Conquer the Peculiarities of Sleep

Will Brain Disorders Be Treated Someday With Tissue Grafts?

Many types of organ transplantations which bordered on experimental only a relatively few years ago are now performed routinely at leading medical centers around the world.

Despite the breadth of the successes which have taken place, one major area of the body remains untouched by the transplant specialist. That region is the brain.

The complexities of the brain and its links to the central nervous system, which includes the spinal cord, and the peripheral nervous system, consisting of the nerves of the body, make it appear that the brain is simply irreplaceable.

In laboratories at the MGH and elsewhere, however, scientists are working on projects which may one day lead to techniques whereby healthy human brain tissue could be implanted in areas of another brain to overcome neurological deficiencies.

Ten years ago, even that suggestion would have raised eyebrows. Connections simply would not form between cells, it was thought. But then a group of investigators in Sweden showed this premise to be false.

During sleep test, device over ear records levels of oxygen in the blood while tube from nose detects air flow.

Using a rat as a model, they lesioned an area in the animal's brain equivalent

(Continued on Page 2)

"Get a good night's sleep, and you'll feel like a new person in the morning."

For most people, these familiar words of assurance hold true. The body feels rejuvenated, the mind more alert.

Why? No one can say for sure. Although up to a third of one's life is spent in sleep, the physiologic events that take place during this period to recharge the human machine remain inadequately defined.

In recent years, however, interest in the sleep process has grown among medical investigators, including specialists at the MGH.

While the majority of Americans enjoy the blessings of sleep, scientists estimate that up to 15 percent of the population suffers from sleeping problems of one kind or another which may impair work performance and social activities.

To help people overcome difficulties arising from disordered sleep and to better understand basic sleep physiology, the MGH has established a Sleep Disorders Clinic and Laboratory.

Underlying the symptoms of insomnia (difficulty initiating or maintaining sleep) or excessive daytime sleepiness may be a potentially treatable medical, neurologic, or psychiatric disorder.

These range from severe anxiety or depression to sleep apnea (a temporary cessation of breathing), nocturnal myoclonus (periodic severe muscle twitching during sleep), nocturnal epilepsy (seizures only at night), narcolepsy (irresistible daytime urge to sleep), sleepwalking, enuresis (loss of bladder control at night), bruxism (grinding of teeth at night), and endocrine disturbances (i.e., hypothyroidism).

The remedy might call for medication; a change of life-style, including

(Continued on Page 4)

Reviewing the Use of Hospital Resources

In the past, physicians caring for patients have enjoyed virtually complete freedom in prescribing tests and treatment. As a consequence of severe cost constraints being placed on hospitals, they may begin to reexamine this tradition.

One cost containment law being tried out in New Jersey is being looked upon as a national model. Under this, a hospital receives a predetermined amount for admitting a patient with a specific diagnosis, regardless of length of stay.

Speaking at a recent meeting of staff physicians, residents, and interns (Medical Grand Rounds), Dr. J. Robert Buchanan, General Director of the MGH, said:

"It doesn't take any imagination to believe that institutions faced with that kind of piecework payment will very rapidly begin to profile the behavior of their physicians to find out which are generating costs way above the national average by which they will be reimbursed." *(Continued on Page 6)*

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206

Martin S. Bander	*Editor*
Myron H. Daniels	*Assistant Editor*
Doris G. Schreckengaust	*Copyreader*

EDITORIAL BOARD

J. Robert Buchanan, MD	*General Director*
Kurt J. Isselbacher, MD	*Research, Medicine*
Paul S. Russell, MD	*Surgery*
Ronald A. Malt, MD	*Surgery*
Roger H. Sweet, MD	*Utilization*
Stanley Bennett	*Photography*
Robert J. Galla	*Designer*

EDITORIAL:

Chapter 372 Has a Positive Side, But. . .

Until now this editorial page has castigated Chapter 372, Massachusetts' new cost control legislation. In the guise of reducing costs, the law has committed some absurdities. On the positive side, though, Chapter 372 has made hospitals explore every crevice for potential cost reductions. To the extent that the state's hospitals have found practical ways to reduce costs, the legislation deserves credit.

Both Chapter 372 and its federal sibling, the new Medicare requirements, will change health care habits. As Dr. J. Robert Buchanan, MGH General Director, points out in a page 1 article, hospitals will be scrutinizing physicians as never before. He predicts that these institutions will develop profiles of doctors' patterns in ordering drugs and tests. The caretakers whose use seems to be above average will have to explain their patterns. For the small number of physicians who tend to overorder, times may soon change.

This is a drastic step. The practice of medicine has traditionally been the sacrosanct privilege of the doctor. As long as the physician can justify his/her practices, the system should remain unchanged. Hospital administrators will have to step in only when a clear abuse arises. Adjudicating borderline situations will require tact and forbearance.

Savings for patients without a concomitant pejorative effect on care is a positive potential from the new laws. But one of the negative realities of 372 has already struck. In the same page 1 article referred to above, Dr. Buchanan describes "the paradox of 1983." The MGH is being forced by the new law to reduce prices while sliding toward an expected deficit of $2 million. For Chapter 372 requires hospitals to limit revenues even while their expenses have increased. The resulting losses will make it difficult to pay bills. As Chapter 372 becomes increasingly strict over the next two years, the problem exacerbates. Some hospitals will either have to lower significantly their quality of care or close their doors. Wonder how the businesses and insurance companies which forced Chapter 372 would enjoy operating under such a law?

Fetal Tissue a Key In Brain Research

(Continued from Page 1)

to that known to be affected in patients with Parkinson's disease. Then they grafted in a segment of the same region from another animal. The new tissue, like that destroyed by the lesion, contained a chemical compound called dopamine, required for the transmittal of certain impulses in the brain. The implant alleviated the abnormal symptoms in the rat.

Scientists learned that while adult tissue could not be grafted successfully into another animal, fetal tissue would work. Not only that, but so long as appropriate fetal tissue was used, it could also be implanted a short distance from the recipient's brain deficiency and still find its way to the correct treatment site.

While the major hurdle to clear in organ transplant surgery is the body's natural tendency to reject foreign tissue, no such rejection threatened the brain implant because of what doctors call the blood brain barrier.

Unlike blood vessels elsewhere in the body, those in the brain have a special makeup. Cells called endothelial cells, which line the walls of the vessels, crowd against each other and also have a special biochemical action. These two factors exclude unwanted substances from the brain, including molecules that are probably important in generating the immune response.

In discussing brain tissue implants at a meeting of colleagues (Medical Grand Rounds), Dr. Mark C. Fishman described the brain as such a privileged site that one can even conduct brain tissue grafts between species, such as mice and rats, without the need for immunosuppressive drugs to guard against rejection.

Dr. Fishman heads The Section on Neurobiology in the MGH's Developmental Biology Laboratory. With a grant from the National Institutes of Health, he is looking into the basic biology of how nerves arrange and rearrange during brain development; also how synapses form. Synapses are spaces across which impulses jump from one nerve (or neuron) to another.

During normal development before birth, cells A connect with cells B by

Photographs: Pages 1, 3, 4 (upper), 5, 6, Myron Daniels; p. 4 (lower), courtesy of Dr. John W. Stakes; p. 8, MGH Photo Lab

Drawing: Page 7, courtesy of Dr. Dean Ornish

Working under sterile conditions, Dr. Mark Fishman removes nerve cells from animal tissue for study of the connections (synapses) between the cells.

virtue of signals which researchers know very little about. For example, when the spinal cord of a chick is surgically turned around, the nerve cells still connect to the muscles that they originally were supposed to go to.

If more than one nerve cell connected with a muscle cell, however, only one nerve cell could stay. The less appropriate connections, or synapses, would be pushed away.

During the first few months of life, the process of synapse elimination is particularly sensitive to the environment.

Citing the work of Drs. David H. Hubel and Torsten N. Wiesel, cowinners of the 1981 Nobel Prize for Medicine, Dr. Fishman explained that if during the critical period one eye of a newborn animal were closed, the input from that eye could be blocked from the cells in the brain, and they would receive only input from the good eye. This would not happen in an adult.

Scientists have worked with a number of diseases in rats to assess the benefits of brain tissue implants.

A rodent called the Brattleboro rat suffers from diabetes insipidus because its brain cannot produce antidiuretic hormone (vasopressin). A grafting of appropriate tissue containing that peptide into the Brattleboro rat would diminish symptoms of diabetes by slowing the rate of drinking and urinating.

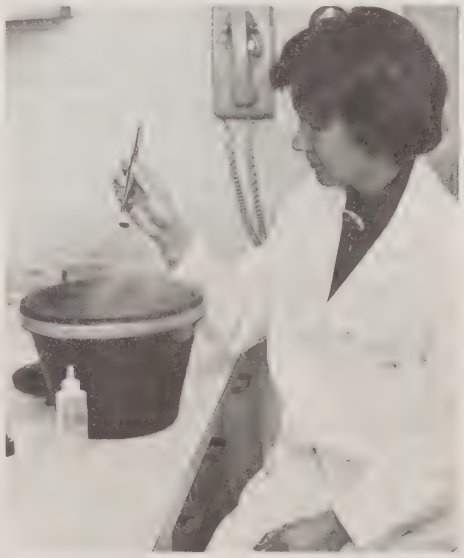
Other rats are born with deficiencies in gonadotropic releasing hormones, important for normal sexual maturation. If one implanted the appropriate neurons from the same area of the brain (the hypothalamus), the testes will descend, sperm production will become normal, and the rats will grow into mature adults.

At the MGH, Dr. Joseph B. Martin, Chief of Neurology, heads a team studying a mouse dwarfed by a deficiency of growth hormone secretion.

"We're trying to do two things," he said. "First, see whether hypothalamic neurons from the normal animal can replace absent function in the genetically dwarfed mouse. Secondly, we would like to identify the way in which that hypothalamic fragment has now signaled the pituitary gland to do its job normally in terms of secreting growth hormone."

Experiments with brain tissue implants have been confined for the most part to mice and rats for a simple reason: their brains are small. Nerve cell implants that have been shown to work had to travel only short distances, at most a few millimeters (each millimeter being about the thickness of a paper clip).

"The implant work is exciting," Dr. Martin said, "in that the nerve cells survive, develop a blood supply, become electrically functional, form synapses, and may restore certain function in a very local range. We still have to solve the problem of how to get those nerve cells to grow to a target more than a few millimeters away."



Research Assistant Margaret Boulos uses liquid nitrogen to freeze and preserve nerve cell specimens pending later study.

Doctors initiated transplant work at one time with monkeys, but the distances confronting the brain implants proved to be a serious handicap.

The problem has to do with regeneration of the central nervous system. The body's peripheral nerves regenerate. When someone, for example, suffers amputation of an arm, surgeons performing a replantation can rejoin a severed nerve, and it will regenerate all the way from the shoulder to the tips of the fingers over a period of months.

"That kind of regeneration doesn't occur in the central nervous system," said Dr. Martin, who is also Bullard Professor of Neurology at Harvard Medical School. "If one cuts the spinal cord, the nerves that are severed actually will sprout, but after going one or two millimeters, the nerves will stop, apparently in response to some inhibitory signal that the nervous system puts out."

Dr. Martin spoke of a former colleague in Canada who conducted interesting experiments on the growth of central nerve cells in animals.

"Dr. Albert Aguayo showed that it is possible for a peripheral nerve to serve as a sort of bridge in the brain," the doctor said.

Suppose, for instance, that a nerve between the brain and the spinal cord were damaged. A segment of peripheral nerve could be inserted into the brain, and some signal from this nerve would cause the cells in the damaged one to sprout and actually grow along the peripheral fibers. The cells might travel two centimeters or more back into the spinal cord before stopping.

Dr. Martin said that if scientists could identify the biochemical activity that takes place to tell nerve cells what they can and cannot do, the investigators might gain a real lead to ways of bringing about full regeneration.

Researchers have many other questions: How does nerve cell A find nerve or muscle cell B? What induces a cell to embrace one connection and reject others? How much tissue would be needed for a graft? Would a small amount grow to fill a larger space?

"We're enthusiastic about the advances that have taken place thus far," said Dr. Martin, "but we've got to learn a lot more about the factors that regulate regeneration. I think we're at least a decade away from doing a brain tissue implantation in a human." ■

Technician Susan Hildreth records vital test data on a sleeping patient while also maintaining a visual check of the patient by means of a TV monitor.

Apnea: A Common Sleep Disorder

(Continued from Page 1)

revised sleeping habits, or surgery. And although the MGH clinic and laboratory operate under the hospital's Neurology Service, the patient's care might require additionally the services of a pulmonary specialist or a psychiatrist.

Dr. John W. Stakes, Director of the Sleep Disorders Clinic and Laboratory, expects apnea to be one of the common problems among newly referred patients.

In this predominantly male disorder, a sleeping person may stop breathing for as long as three minutes, he said, because (1) the brain's influence upon muscles operating the lungs in a rhythmic fashion somehow becomes interrupted (central apnea), and/or (2) the upper airway becomes blocked (obstructive apnea).

As many as several hundred apneic episodes may occur during a night, each resumption of breathing accompanied by a loud, raucous snore as the individual gasps for air.

Although the spouse is aware of heavy snoring, the patient may be entirely oblivious to these apneas. Recordings of sleep have shown frequent transient awakenings with apneic events, thus dramatically reducing the amount of restful sleep and resulting in daytime sleepiness. With apnea the blood oxygen level may drop severely, carbon dioxide levels may rise, and disturbances of heart rhythm may occur. Untreated, sleep apnea may result in pulmonary hypertension and heart failure.

"In obstructive apnea, the major problem often is laxity of upper airway muscles, such as those of the tongue, pharynx [throat], or larynx [vocal cords]," said Dr. David J. Kanarek, a member of the Pulmonary Unit who is also associated with the Sleep Laboratory. "When one tries to take a deep breath, negative pressure is generated in the airways which causes the muscles to collapse."

Only after the muscles regain their tone and the airways reopen, he said, can the oxygen and carbon dioxide concentrations return to normal.

To diagnose apnea, a physician might ask a patient to spend one or two nights sleeping in a quiet, darkened room in the sleep laboratory.

Depending on the extent of data needed, specialists might attach surface electrodes to monitor brain wave activity, eye and muscle movements, and heart rhythm; also, devices to record body temperature fluctuations, air flow at nose and mouth, chest movements, and oxygen saturation of the blood. All of the tests are noninvasive.

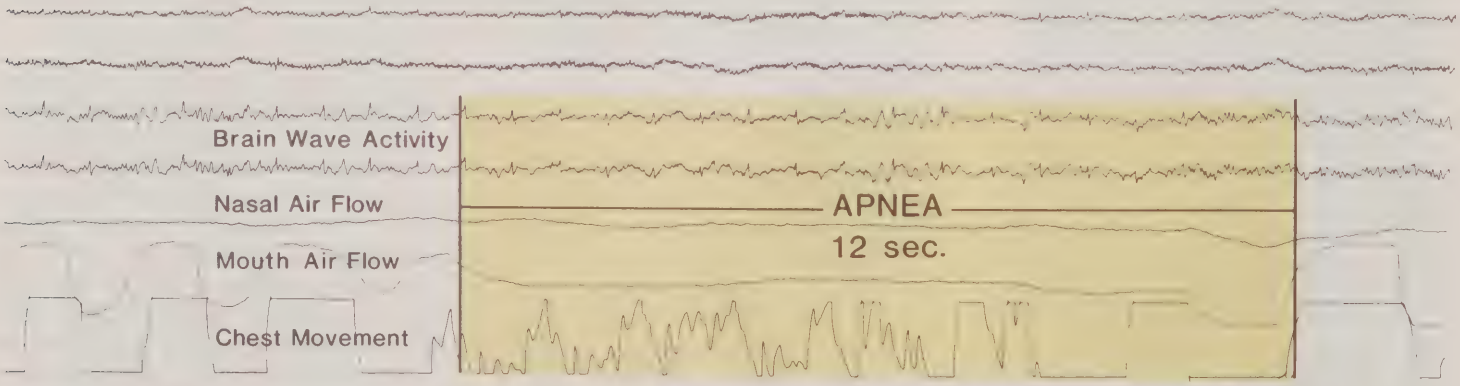
"Much quantitative information regarding sleep efficiency, 'depth' of sleep, and REM [rapid eye movement]-related apnea can be derived from recording the frequent and dramatic changes in brain wave activity during sleep," Dr. Stakes said. Also daytime excessive somnolence can be quantitated in apneic patients.

One of the most common treatments for obstructive apnea is a tracheotomy, a procedure whereby the surgeon makes an artificial opening in a person's trachea, or windpipe, thus enabling him to breathe by bypassing the obstruction.

Since the body prevents apnea from developing during waking hours by keeping airway muscles well toned, the patient can keep the surgical opening covered until he goes to bed.

Surgery of another kind may be in order for the apneic patient. A middle-aged physicist, for example, snored so loudly that occupants of neighboring apartments complained. He got so little rest that he often dozed in his car, at church, and during business conferences. For a time, he feared loss of his job.

A retruded chin apparently precipi-



EEG (Electroencephalograph) recording of sleeping patient shows a 12-second stoppage of breathing (apnea). Although brain wave activity remained unchanged, note absence of air flow from mouth and irregular, ineffective chest movements during this period. Lack of nasal air flow throughout recording indicates patient was a mouth breather.

tated his dilemma by causing his tongue to block his airway. Surgical correction of the jaw usually cures the breathing difficulty. Doctors perform 35 or 40 of these operations at the MGH each year.

The dramatic effects of narcolepsy, a disorder which can make a person so drowsy he might suddenly fall asleep while eating, or dancing, or even making love, have been well publicized. Not so well known, however, is a symptom which eventually affects all narcoleptics. That is cataplexy.

Cataplexy represents a sudden loss of muscle power, usually triggered by some strong emotion such as anger, surprise, or laughter. During cataplectic attacks, which may last from several seconds to two minutes or longer, the individual usually remains fully conscious.

Dr. Stakes told of a cataplectic patient who spotted a 10 dollar bill on a sidewalk but lost all muscle tone as he approached the money. He could not get near enough to the bill to pick it up and wound up sitting on the curb, a picture of frustration.

Scientists describe the sleepiness brought on by narcolepsy as an attack of REM sleep occurring outside of the normal sleep cycle.

When a healthy person sleeps, he first experiences about 90 minutes of non-REM sleep, then goes into a REM period when he begins to dream. The REM phase occurs about 4–5 times a night.

Upon falling asleep, the narcoleptic apparently enters immediately into the REM phase. Although his body becomes limp, his brain remains quite active, sometimes experiencing episodes of visual hallucinations. A momentary sensation of paralysis in arms or legs may also occur.

Doctors often prescribe an antidepressant (i.e., imipramine) for cataplexy and a stimulant (i.e., methylphenidate) for the sleepiness. Dr. Stakes said the Sleep Disorders Clinic hopes to conduct controlled trials of medications in patients with narcolepsy.

Just as most people who snore are perfectly normal, so are most folks who occasionally have trouble falling or staying asleep. When sleeping becomes difficult every night, the condition known as insomnia is suspected.

Worry, anxiety, and depression all contribute to insomnia, making its treatment a task for the psychiatrist.

Dr. Ned H. Cassem, an MGH psychiatrist who has studied sleep disorders for years, said that, as in narcolepsy, early dreaming once the patient dozes

Using a computer, Dr. Keith Chiappa interprets signals recorded during nightlong sleep test.

can be a sign of depression.

"If you prevent those REM periods by depriving the person of sleep all night, you sometimes find that he feels remarkably well the next day," Dr. Cassem said.

Sleep researchers argue against the general use of sleeping pills to curb insomnia. While they may be useful in treating someone whose insomnia can be attributed to a temporarily stressful condition, the pills can become habit-forming and less effective over time.

. . . Up to 15 percent of the population suffers from sleeping problems of one kind or another. . .

Some forms of insomnia may stem from a disturbance of the body's so-called biological clock (*MGH News,* October 1979). By going to bed 2–3 hours later each night, one can manipulate the sleep-wake cycle until it is back to a socially acceptable, normal time.

One of Dr. Cassem's special interests is the study of sleep disorders among heart surgery patients. He said investigators have found that the more severe the illness or the more complex the surgical work, the more likely the patient will suffer from delirium.

Dr. Cassem said he found it intriguing that at the Cleveland Clinic where many heart operations take place, the rate of postsurgical delirium is low.

"Surgeons there have the impression that multiple operations scheduled at the same time, with patients going to the recovery room at about the same time, account for the lower delirium rate," Dr. Cassem declared.

"The patients enter surgery more aware that they are not alone in their predicament. Later, in recovery, they clearly appear less disoriented."

In most instances, those who become delirious after heart surgery recover completely and have no aftereffects.

Dr. Cassem and a colleague in the MGH Psychiatry Service, Dr. George B. Murray, are expected to play an active role in the work of the Sleep Laboratory.

Air travel across time zones, changes in work shifts, aging. . . The potential causes of sleep disorders go on.

Dr. Stakes, who is both a neurologist and internist, said patients undergoing sleep laboratory testing may be referred through the Sleep Disorders Clinic, a part of the MGH Neurology Clinic, or by other physicians in or outside the hospital. Test results will be available in two weeks.

The sleep rooms are situated in the Clinical Neurophysiology Laboratory, directed by Dr. Robert R. Young. Dr. Keith H. Chiappa, head of the Brain Wave Laboratory, assists in the analysis of the signals recorded during the all-night sleep testing. Dr. William Schwartz, a neurologist and researcher, also works closely with Dr. Stakes on sleep studies.

There is much to learn. Why, for instance, do some people have nightmares? What drugs can have adverse effects on sleep? And does the average person need as many as eight hours of sleep at night?

Edison and Napoleon got just four or five hours of nightly rest, and they did just fine. ■

Confronted With a Fiscal Dilemma

(Continued from Page 1)

Dr. Buchanan emphasized to the assembly that the MGH "must start examining carefully and collectively the utilization of expensive resources for the care of our patients because only in that way are we going to be able to preserve the traditions and greatness of an institution like this one."

Ironically, the MGH has reduced patient charges, ranging from room rates to operating facilities to radiologic procedures, by seven percent across the board while at the same time heading toward a probable year-end operating deficit of some $2 million.

"I call it the paradox of 1983," Dr. Buchanan declared.

In reality, because of increased activities such as the performance of more ancillary (support) services, MGH revenue would have wound up $12 million above budget if this price reduction had not taken place.

Why then a deficit? The answer lies in a convoluted new Massachusetts law which aims at hospital cost constraints but has produced confusion.

For one thing, Dr. Buchanan explained, "The state has said, 'You can't have that $12 million. It exceeds your cap [a government-imposed limit on revenues].'"

Secondly, the additional volume of hospital activity generated new expenses. Even though the MGH cannot retain the added revenue, the institution must still absorb the added costs.

"We have to have something greater than a four percent increase in inpatient ancillaries before we are eligible for any new reimbursement for the performance of those ancillary services," Dr. Buchanan said, "and even then we only get 25 percent of the incremental costs of doing the additional tests."

The costs to hospitals in rendering hospital care continue to increase in many ways.

In oncology (tumor medicine) alone, expenses for drugs increased during fiscal 1981–82 by more than a quarter of a million dollars over the preceding year. In the Hyperalimentation Unit, which specializes in the delivery of nutriments intravenously, the number of bottles used per day has risen from 60 in 1981 to 160 at present.

As of April 1 the hospital's malpractice insurance premiums under joint coverage with other Harvard-affiliated hospitals jumped by 40 percent, almost half a million dollars.

The costs of certain operations declined dramatically after a generous gift by the Cabot Family Charitable Trust helped to create the Cabot Day Surgery Floor at the MGH.

Passage in the mid 1960s of the Medicare and Medicaid programs to give the poor and elderly access to high quality medical care has had a significant effect on hospital operations.

When the programs came into existence, Dr. Buchanan said, hospitals were told, "'These patients have got to be in the mainstream of your institutional life in every respect.'

"As we now face cutbacks from governmental reimbursement for those programs," he declared, "we find it virtually impossible to reduce services which are used predominantly by those two cohorts of patients."

The General Director pointed out that although individuals aged 65 and older represent only about 13 percent of the nation's population, health care costs for the senior citizens account for about 33 percent of total expenditures.

"It is well recognized," he said, "that this segment of our population is bound to grow, and very rapidly. We have to be concerned that the numbers of young workers upon whom the tax is placed for the support of that program will not grow at the same rate of speed as that of the elderly population."

The mid 1960s also saw government passage of a Health Professions Education Assistance Act which sought to stimulate medical school enrollment by providing loans, scholarships, and capitation support. The new law doubled the enrollment between 1967 and 1977. Each year some 18,000 new physicians practice medicine.

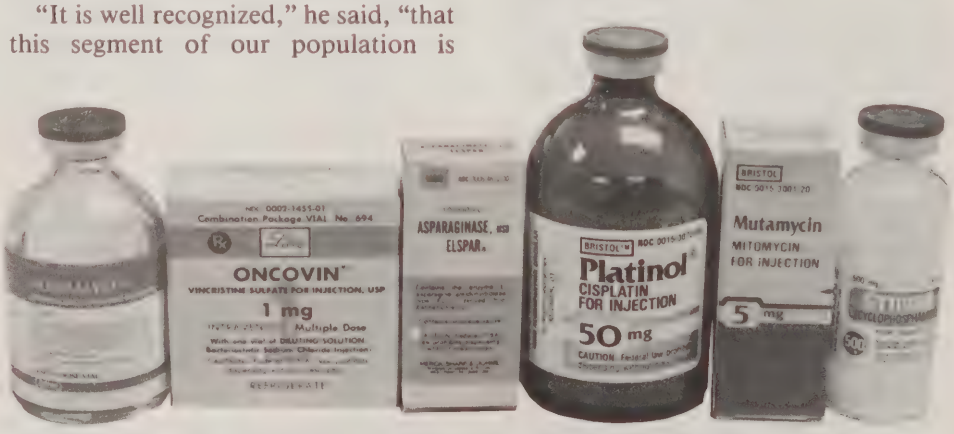
Dr. Buchanan said, however, that with the success of the program may have come new problems since economists judge that each new physician generates somewhere between $250,000 and $300,000 of additional health care expense annually.

The Massachusetts health care cost containment law known as Chapter 372 establishes criteria for increases in hospital budgets.

The statute provides that an index shall be calculated relative to the amount of inflation affecting goods and services bought by hospitals. "With that computed for each of the next couple of years," Dr. Buchanan told his colleagues, "we are informed we will be allowed two percent less increase in our budget than the index would suggest because we are expected to make up the two percent by being more productive and more effective."

He said the kinds of rate increases experienced in the past are now history and no longer will be reflected in the MGH's operating budget, including generous wage and salary hikes for employees. "We won't be alone in that," he added. "I suspect that will be commonplace in the Commonwealth."

Dr. Buchanan reminded his listeners that 65 percent of what the MGH spends



During the past fiscal year, the use of anticancer drugs alone cost an added $250,000 at the MGH.

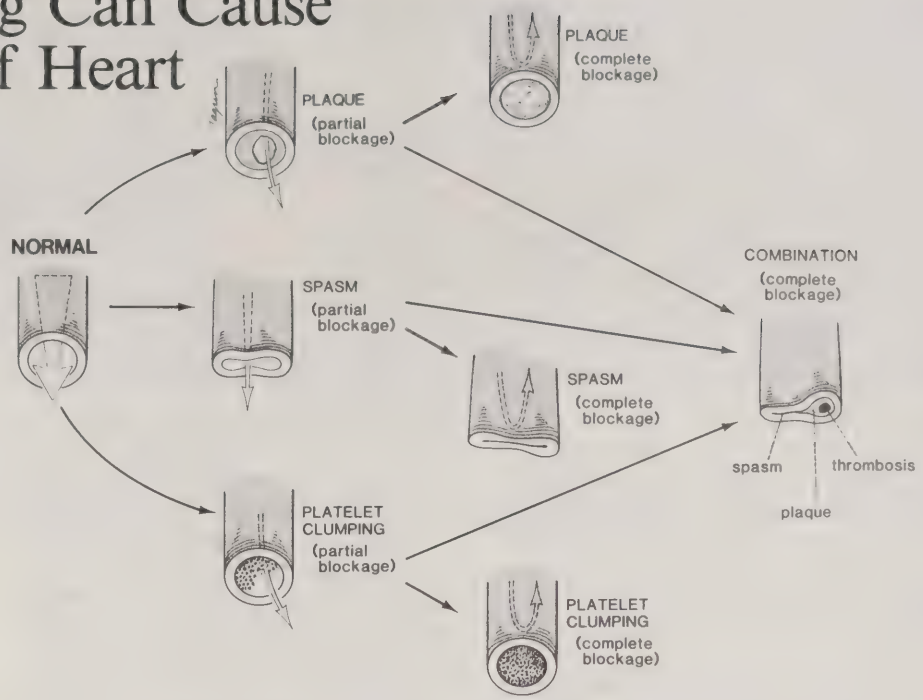
Spasms and Clotting Can Cause Sudden Stoppage of Heart

A severe reduction of blood flow to the heart, causing it to starve for oxygen, accounts for a vast majority of the deaths attributed each year to heart disease, America's leading killer.

The heartbeat becomes irregular and progresses to a completely disorganized state called ventricular fibrillation. The heart no longer can pump effectively. Since the brain cannot live without blood and oxygen for more than a few minutes, the patient dies.

A gradual buildup of fatty material (plaque) in the lining of the coronary arteries, like rust in a pipe, was long thought to be the chief reason for the reduction of blood flow to the heart in coronary heart disease.

Surprisingly, however, some 60 percent of those who die from this disease are stricken suddenly, often without a hint of a developing disorder.



Various ways in which blood flow through coronary arteries can become blocked

In recent years, investigators have documented two developments that help explain the suddenness with which the heart is sometimes stricken.

Smooth muscles lining the coronary arteries may go into spasm and obstruct blood flow. Also, platelets, the main clotting factor in blood, may contribute to a vessel blockage by clumping. The more a coronary artery is obstructed by plaque the less coronary artery spasm and/or platelet clumping is required to completely block coronary blood flow.

A diet high in fat and cholesterol may generate both spasms and platelet clumping by causing platelets to secrete excessive amounts of a substance called thromboxane, a potent constrictor of blood vessels. Thromboxane stimulates clotting (*MGH News,* December 1981).

Spasms and clumping can also result from stress on the body's sympathetic nervous system. This is a network of nerves (autonomic) which involuntarily influence body organs, such as by narrowing blood vessels during mental or physical strain.

The physiologic changes precipitated by stress constitute what doctors term a "fight-or-flight" response. If a person were wounded in battle, arterial spasm and platelet clumping would help to stop the bleeding faster.

"In today's life-style, these survival mechanisms may become destructive because we chronically activate them," said Dr. Dean Ornish, a physician at the MGH. "We eat meals high in fat and cholesterol three times a day. We seem almost continually under stress. And we don't exercise enough."

A second-year Resident on the MGH Medical Services and a Clinical Fellow in Medicine at Harvard Medical School, Dr. Ornish studied coronary heart patients in 1977 and 1980 while at the

(Concluded on Page 8)

is for personnel, and that much of the so-called nonpeople expenses relate to things such as debt service on loans, malpractice insurance premiums, and the cost of steam purchased from Boston Edison, items which cannot be influenced to any appreciable degree.

To live within the constraints imposed by law, the hospital has sought to save about $5 million through nonreplacement of personnel leaving the institution. But the effort has not been successful. Whereas in the past some 40 of the 8,500 full-time equivalent jobs terminated each week, only three or four employees now leave the hospital weekly.

People often ask, "Why are you putting up this building?" or "Why are you installing this new equipment?" when you have a serious operating budget problem.

"There is a major difference between an operating budget and a capital budget," Dr. Buchanan said. "We are not allowed to switch dollars.

"Most people who donate money to us are not interested in supporting our routine activities. They believe that the government and third-party carriers are doing that adequately. They want their dollars spent in a very special way, frequently on capital items."

Dr. Buchanan said he hopes that since the MGH is a referral hospital some kind of new criteria eventually will evolve that will govern reimbursements to teaching institutions more favorably than present regulations.

"It does not make sense for us to say that our destiny is bread-and-butter medicine, not with the armamentarium of talent that we have here," he declared.

The MGH General Director said he frankly does not know how long the hospital will be able to maintain its "noble tradition of taking care of all comers."

"Part of Chapter 372 puts a cap on the amount of free care and bad debt for which the institution can be reimbursed," he pointed out. "If other institutions decide that it is in their economic interest to start screening out admissions that are likely to end up as free care and bad debt and refer them elsewhere, like to us, we would be inundated. We then would have to take the posture that we are no better able to absorb that unreimbursed expense than anybody else." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Aiding the Heart With a Proper Life-Style

(Concluded from Page 7)

Baylor College of Medicine in Houston, Texas. Working under grants from Gerald D. Hines Interests and the National Institutes of Health, he found that a combination of simple stress management techniques and dietary changes may often quickly improve heart function.

Dr. Ornish's program and why and how it works are detailed in a book he authored, *Stress, Diet, & Your Heart,* recently published by Holt, Rinehart, and Winston, of New York.

In the 1977 study, the results of which were published in the scientific journal, *Clinical Research,* Dr. Ornish followed 10 heart patients, many of whom were experiencing daily episodes of chest pains (angina) because of poor blood flow to the heart.

He discovered that after only one month under this program a substantial number of the patients became pain-free and were able to return to a full workweek for the first time in years. Measurements of blood pressure, cholesterol, and duration of exercise capability all improved.

A nuclear (thallium) imaging scan conducted on several of the patients demonstrated initially an inadequate blood flow through the heart with congestion in the lungs. Follow-up scans a month later revealed much more normal pictures.

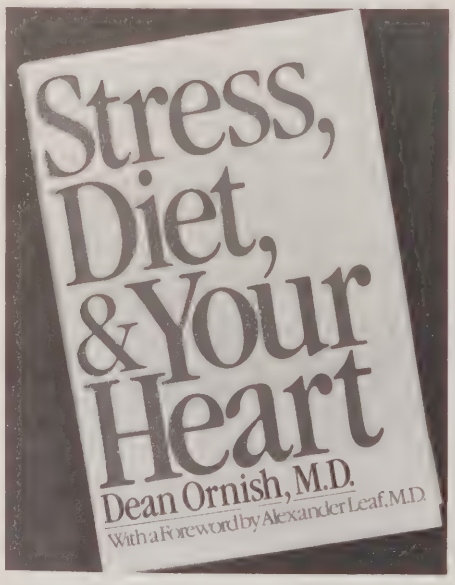
In 1980 the doctor and his colleagues conducted a detailed study involving 46 patients. Half underwent the program. The remainder served as a control group for comparing any changes noted in the other patients.

The results, published this year in the *Journal of the American Medical Association,* again revealed marked improvements. This time a nuclear technique called gated blood pool scanning permitted a quantitative assessment of how well the heart pumped blood, both at rest and during exercise.

The investigators reported that at the end of 24 days tests showed the heart of many of the program participants contracted more uniformly and could pump blood more normally. Angina pain declined in frequency by 91 percent. Exercise capability improved by 44 percent. Blood pressure measurements, taken during rest and while under stress, were better. Cholesterol readings fell 21 percent. Total work capability (on a bicycle) improved 55 percent.

"We have been conditioned to think that something has to be new and expensive, a product of high technology, to be effective," Dr. Ornish said. "It is sometimes hard to believe that things as simple as stress management training, changes in diet, and cessation of smoking can be so useful, even in the short run.

"Drugs and surgery can, of course, be lifesaving, but they do little about the causes of the problem. For example, if someone undergoes a bypass operation and, because he feels better, resumes eating foods high in fat and cholesterol, turns again to smoking, and continues to lead a stressful life, the bypass grafts may begin to clog."



A program for treating and helping to prevent coronary heart disease

By addressing the causes of the problem, the doctor declared, the need for drugs and surgery sometimes may be reduced. If required, they may have even greater effectiveness.

Stress comes not only from the environment but also from how an individual reacts to it. He can learn how to react to what could be stressful situations in ways that are less so, becoming even more productive while enjoying life more.

Many people are unaware of chronic tension until the end of the day when their neck or back hurts. A few minutes of gentle stretching can ease the tension in muscle fibers.

Meditating helps to produce a relaxed state. The technique simply means focusing one's awareness for a few minutes on something soothing, such as a sound, word, or calming scene.

Taking a few minutes periodically to breathe more slowly and deeply also can ease tensions. Ever notice a professional basketball player just before he attempts a free throw? Typically, he takes a deep breath.

On diet changes, Dr. Ornish's book categorizes foods into five groups ranging from items highest in fat and cholesterol (number five) to only plant-based foods low in fat and containing no cholesterol (number one).

"Rather than altering one's diet radically," the doctor said, "we recommend that an individual find a place on the spectrum, and to the degree that he can move in the Group One direction, the risk of developing coronary heart disease may be reduced."

To further encourage a switch to more appropriate meal planning, the book lists many recipes for attractive and tasty repasts.

Dr. Ornish cautioned that "the program is a complement to — not a substitute for — medical care. Anyone taking medication or with coronary heart disease should consult with his physician before embarking on the various recommended programs." ■

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 42 No. 5 June–August, 1983

Latest Laser Techniques Expand Health Care Skills

Animals, Too, Reap The Many Benefits Of Medical Testing

Diabetes is not only a disease of man, it affects most mammals – dogs, cats, monkeys, even dolphins to name just a few.

Fortunately help is readily available. Insulin, discovered in 1922 through a series of experiments in dogs, is proving to be as successful in the treatment of animal diabetes as it has been in treating the disease in man.

The treatment of diabetes is only one area in which animals have gained from research originally performed on animals to benefit man. Puppies are inoculated with measles vaccine to protect them from canine distemper during the first months of life. As they grow older, animals may receive antibiotics for infections, medication for a sluggish thyroid, phenytoin (Dilantin) to control seizures, and diuretics for heart disease.

Efforts to rehabilitate injured or sick endangered species and marine mammals have involved CT scans and Nuclear Magnetic Resonance (NMR), two of the most sophisticated diagnostic tools available, and complex surgical procedures.

The use of animals in medical research has been a boon to mankind, and man has in return applied the knowledge gained in this work to improve the quality and length of life of the animals themselves.

Yet, there is a growing movement in this country to end or seriously curtail animal research. Some organized groups contend that there is no need to con-

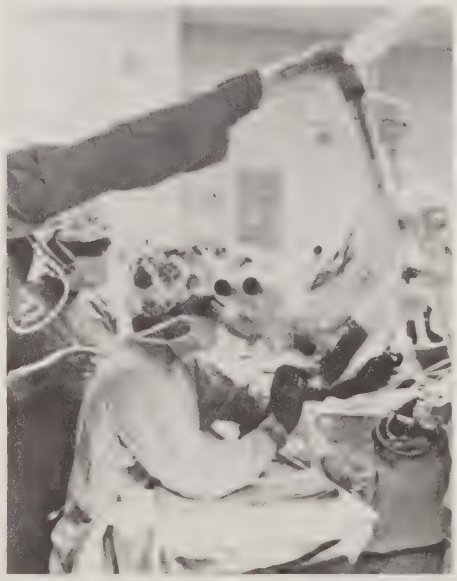
(Continued on Page 2)

Although more than 20 years have passed since science gave birth to the laser, its versatility in helping doctors to treat human ills is just now being realized.

In one respect immensely powerful because of large amounts of energy being packed into a narrow beam of light, the laser at the same time can be exquisitely gentle.

The combination of these factors has made it possible for patients at the MGH to undergo certain delicate neurosurgical procedures at less risk than before.

Addressing a gathering of colleagues (Medical Grand Rounds) on use of the carbon dioxide (CO_2) laser – sometimes referred to as a "knife of light" – Dr. Robert L. Martuza, an MGH neurosurgeon, told of a neurofibromatosis patient who had tumors pressing on his spinal cord, causing a progressive paralysis.



Drs. Nicholas T. Zervas, Chief of Neurosurgery, (left), and Robert L. Martuza use a CO_2 laser connected to an operating microscope to remove a tumor from a patient's brain.

Neurofibromatosis (*MGH News,* October 1980) is a malady of genetic origin which can lead to multiple tumors wherever nerves travel in the body.

It was clear that because of the pressure exerted by the tumors, their removal would entail some manipulation of the spinal cord, with accompanying increased risk to the patient.

"By applying a moistened cotton pad, the normal spinal cord can be protected from the laser beam and then the CO_2 laser can be used to vaporize each tumor," Dr. Martuza told the assembled physicians.

The moistening, coupled with the fact that tissue itself consists largely of water, reduces the risk to the patient because the carbon dioxide laser cannot penetrate water by more than a fraction of a millimeter (1/25 inch).

Used in neurosurgery at the MGH for the past year and a half, the laser has also proved valuable in the removal of other kinds of tumors, such as meningiomas which affect one or more of the membranes covering the brain.

The surgeon, who often works with an operating microscope, cannot see the CO_2 laser beam because its wavelength is invisible to humans.

However, the surgeon is able to compensate for this. He aims a very low-powered, helium-neon laser along the same pathway as that of the CO_2. Since both lasers are built into the same unit, the doctor knows that once he has focused the helium-neon's red light the CO_2 beam will also be on target.

"The laser is not appropriate for all neurosurgical uses," Dr. Martuza said.

(Continued on Page 4)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114 Telephone (617) 726-2206

Martin S. Bander	*Editor*
Myron H. Daniels	*Assistant Editor*
Doris G. Schreckengaust	*Copyreader*

EDITORIAL BOARD

J. Robert Buchanan, MD	*General Director*
Kurt J. Isselbacher, MD	*Research, Medicine*
Paul S. Russell, MD	*Surgery*
Ronald A. Malt, MD	*Surgery*
Roger H. Sweet, MD	*Utilization*
Stanley Bennett	*Photography*
Robert J. Galla	*Designer*

EDITORIAL: Animal Research — a Perspective

Each year animal pounds put to death an estimated 10 to 20 million dogs and cats. Those numbers contrast with about 260,000 dogs and cats used annually in research. Animals killed in pounds die essentially because they have been abandoned. Their deaths serve no purpose except to do away with unwanted pets. For the other 260,000 dogs and cats, government regulations protect them from abuses. Anesthesia renders them free from the pain of surgery. They live in quarters that must be clean and meet minimum space standards.

All of which is not to claim that research animals live idyllic lives. Even with anesthesia there may be pain during the recuperative phase of some experimental procedures. And given a choice, animals would no more want to spend their days in laboratory cages than in pound cages. What's worse, occasional researchers disobey regulations, and the animals suffer. Fortunately such instances seem to be exceptions, and once discovered research money can be withheld.

The basic purpose of biomedical animal research is to find better ways to diagnose, treat, and cure disease. A page 1 article describes a few of the thousands of resulting advances that redound to patients. Without animal studies medicine would still consist of leeches and placebos. The irony focused on by the page 1 article is that animals themselves have benefited. And will continue to benefit.

What are the alternatives to animal studies? One could stop research and let medicine stagnate and indeed regress. One could use human subjects before animal studies indicate a project's safety, but how many of us would volunteer for such experiments? One could seek alternatives to both humans and animals. As technology marches forward, scientists will develop many substitute methods. To the extent possible we should avail ourselves of these new technologies. At the same time we should avoid at all cost employing unscientific substitutes that will spare animals but cause untold suffering to the human race. Do we really want to save rats and cats today at the expense of parents and children tomorrow?

Animal welfare organizations existed in the 19th century. They began in England and centered their original attention on horses. Animal research as we know it evolved later. It would be sad to subvert the original aims of animal welfare to the detriment of both mankind and the animal world.

Letters to the Editor

[Editor's Note.]

The MGH News *has received two letters pointing out correctly a statistical error in the April editorial on hospital costs. In computing the average annual cost of inflation for randomly selected supplies bought by the hospital, the* News *divided the total cost increase by the number of years involved. For example, we listed an item that rose from $413.19 to $1,126.85, "a leap of 273 percent" since 1972 or "27 percent a year." The 273 percent is correct. However, because of the compounding effect, the average yearly inflation is less than half of 27 percent a year — still high but considerably lower than stated.*

One of the letter writers, Norman F. Beach of Nantucket, added: "The charges made by hospitals to patients or third-party payers have risen over the last decade at least as dramatically as the cost of supplies. A semiprivate room at the small rural hospital with which I'm associated as a trustee has increased from $40 in 1974 to $215 in 1983 (and we still lose money). This is a 10-year increase of 537 percent, an average annual increase of just over 20 percent (not 54 percent). We are all, suppliers, intermediaries, and users alike, caught in the same inflationary bind, but the hospitals are certainly not holier than the rest of us. Perhaps you'd like publicly to compare your rates today with those of 10 years ago."

*****

In 1973 the MGH had a single semiprivate room charge of $104, and in 1974 — $125. Today the hospital's semiprivate rate ranges from $237 to $265.

Heart Care Gained With Animal Trials

(Continued from Page 1)

duct medical research in animals, that there are alternate methods available that will yield the same results.

The truth is that although alternates are useful in certain instances, the technology is not yet available and in some cases may never be available to replace animals completely in medical research. Sometimes the only substitute for an animal is a human being.

"The success of cardiac surgery as we know it today is largely due to work in animal models," said Dr. W. John Powell, Jr., an MGH cardiologist and the Department of Medicine's representative to the MGH Subcommittee on Animal Care. "Methods of preserving the heart during surgery using low temperatures, high potassium solutions, and other chemical solutions were all developed in the animal model."

In fact, the modern era of open-heart surgery began in 1944 when doctors in Baltimore corrected an abnormality in the blood vessels leading into and out of the heart of a year-old baby weighing only ten pounds. The idea for the so-called "blue-baby operation" was conceived four years earlier, but doctors first had to test and then perfect the procedure in animals before operating on a sick child.

"Whenever we perform a new surgical technique on a human being, we want to make sure that the procedure has been tested on animals first," said Dr. Ronald W. Lamont-Havers, Executive Secretary to the MGH Committee

---

Photographs: Page 1, courtesy of Dr. Robert L. Martuza; all others by Myron Daniels.

Drawings: Page 7 (left), from Heidi's Horse by Sylvia Fein, Exelrod Press, Pleasant Hill, CA; p. 7 (right), © SPADEM, Paris/VAGA, New York, 1983; p. 8 (left), from Nadia: A Case of Extraordinary Drawing Ability in an Autistic Child, by Dr. Lorna Selfe, © 1977 by Academic Press, Inc., London; p. 8 (right), reproduced by gracious permission of Her Majesty Queen Elizabeth II

on Research. "You wouldn't want surgeons doing their first liver transplant on a baby without knowing that they had practiced it on an animal and developed their skills of hooking up the liver to the small blood vessels leading into and out of it."

The development of new surgical techniques is the most striking example of the importance and irreplaceability of animals in medical research. The fields of heart and transplantation surgery are perhaps the best known, but there are many others. Experiments are being conducted to make better artificial hips and to develop new artificial joints needed by people crippled by arthritis or injury. Newly improved endotrachial tubes, the airway pipes used in intensive care units and during surgery to support breathing, must be tried out in animals before they can be used in man. So was the artificial heart employed in Utah.

Another area in which animal research is crucial to medicine is in testing the safety and effectiveness of drugs.

"You cannot develop drugs in tissue cultures that do not have livers to metabolize them and kidneys to excrete them," said Dr. Warren M. Zapol, an MGH anesthesiologist. "How can you give to a human a new radioactive drug that you have only tested in tissue culture? How do you know whether it will be excreted or stay in the man forever? How do you know where and how long it will remain in the body, and how much radiation it will deliver?"

Over the past five years there has been a shift toward the use of tissue cultures in tests to determine whether certain drugs or chemicals cause cancer, genetic changes, or injure certain organs. Although tissue culture studies have proven their effectiveness in this area, other such studies are applicable to humans only when the cultured cells react as cells would in an intact organ.

For example, heart cells grown in culture and subjected to low oxygen will provide some information on the biochemistry and behavior of oxygen-deprived heart cells. But when the beating heart is deprived of oxygen, the heart is unable to flush out the byproducts of metabolism, which are also injurious to heart function. In a tissue culture these byproducts diffuse away from the heart cells into the fluid surrounding the tissue and thus do not have the added detrimental effect that they have in the patient's intact heart.

"In the area of heart research, tissue culture studies provide some useful information, but the data would still have to be confirmed in animals," said Dr. Powell, who is also an Associate Professor of Medicine at Harvard Medical School. "It would be irresponsible to take data from tissue culture and apply it directly to man."

Easily keeping up with her owner, Dr. Richard Erbe, despite the human equivalent of 84 years of age, Muffy typified countless animals kept in good health by medical care made possible through animal research.

Mathematical modeling and computer simulations are other alternates to animal research that are used in certain instances. But, as remarkable as the current crop of computers are, to run their programs scientists still have to provide the computers with data obtained from animals or humans.

Perhaps one of the best safeguards against the overuse or abuse of animals in research is their expense. "I don't think that anyone likes to use animals unless it is really necessary," said Dr. Lamont-Havers. "For another thing, they are very expensive, and we prefer to look for less expensive ways of getting information. But, when it comes right down to it, there is certain information that we can only obtain through animal studies."

There are other checks and balances to insure that animals are treated humanely and not used unnecessarily in research. "People who propose to carry out experiments in animals must meet certain standards for animal care set by the National Institutes of Health (NIH), and they must compete for dwindling funds," said Dr. Powell. "And the big factor in determining who gets funding is how important the research is."

Guidelines established by the NIH and the American Physiological Society state the conditions under which experiments in animals may take place. And the U.S. Department of Agriculture inspects the animal areas with no prior warning. In addition, the MGH has implemented its own system to protect animals used in research at the hospital.

The MGH has established a subcommittee of its Committee on Research to evaluate all proposed experiments using animals. The committee members examine each protocol to determine whether the animal species is appropriate, and whether necessary safeguards will be taken to protect the animal from pain.

"We are in effect looking at the use of animals in much the same way that we look at the use of human research," said Dr. Lamont-Havers. "Our committee has hospital representatives, community representatives including a member of the Massachusetts Society for the Prevention of Cruelty to Animals, and a veterinarian who go over all protocols before they are approved."

Many different animal species are required to do medical research because no one animal is just like man. For example, calves and dogs are used for cardiovascular research because their hearts and blood vessels are most similar to man's, and the majority of neurological research is done in cats because their nerve structure resembles man's.

"Animals are different from man,

(Concluded on Page 4)

Each Type of Laser Offers Unique Effect

(Continued from Page 1)

"In most situations, it works more slowly than other instruments, but, in selected instances, the laser does offer advantages.

"Since the CO_2 touches only the surface of exposed tissue, the surgeon can see everything that takes place. The laser also permits the removal of tumors with decreased bleeding. And since this beam of light does not interfere with other surgical instruments, surgery can often be performed through a smaller opening."

Dr. Martuza said that although the CO_2 laser is now of only limited use in neurosurgery the device represents only one of an impressive array of tools that fire beams of radiant energy which ultimately will expand the applications of lasers in medicine and surgery.

"The particular combination of properties is quantitatively different in each laser, and this causes qualitatively different effects on living tissue," said Dr. John A. Parrish, Director of the MGH Dermatology Department's Wellman Research Laboratories, which include a recently opened laser laboratory.

Lasers have four qualities that distinguish them from most other light sources, such as fluorescent lighting and sunlight.

A laser's most impressive quality is its exceptionally high *intensity,* or heat, sufficient to evaporate or boil away tissue. Lasers also have *monochromaticity,* which means that each device operates on a particular wavelength, emitting radiation that affects only specific tissue.

Light is said to have *coherence* when its electric and magnetic fields are perfectly in phase with one another. This allows the instrument's power to be focused on sites as minute as a specific chromosome within a cell.

And lasers can release energy in either very short *pulses* or as a continuous beam. The duration of a pulse (pulse width) may be as brief as a trillionth of a second.

In the past, most medical applications of lasers have hinged on their high intensity. *MGH studies, published April 29th in* Science Magazine, *provided evidence that when monochromatic light at short pulse width is used in conjunction with specific absorption of this energy by targets, the thermal effects of the laser can be confined to the tiniest structures within tissue.*

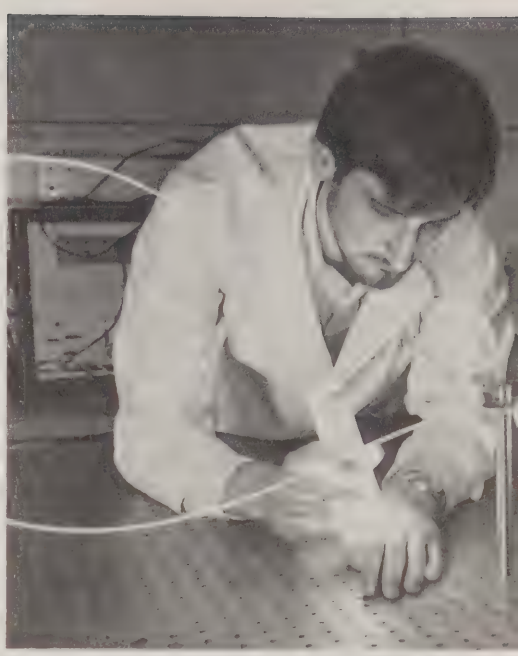
Coauthored by R. Rox Anderson, a long-time member of the photomedicine research team and a Harvard Medical School student, and by Dr. Parrish, the journal article described how in both an animal model and in human skin a laser ray affected targeted blood vessels and pigment granules in the skin (melanosomes) without harming other surrounding tissue.

When the various laser properties are carefully coordinated, the beam needs to be turned on for a very brief period, so brief that the target can actually heat up and cool off before the thermal energy can reach adjacent structures. It is even possible to alter a component of a cell without harming the rest of the cell.

Since each laser has unique characteristics, Dr. Parrish said, a principal goal of his laser laboratory is "to determine how to best utilize their varying properties for cutting through tissue. We hope ultimately to find ways of destroying diseased tissue including certain cancers through the powerfully concentrated light of the laser."

Currently occupying temporary quarters, the Wellman Research Laboratories will move into a permanent home on completion of the hospital's new 11-story Wellman Research Building.

Plans for the building progressed in February 1981 when Arthur O. Wellman and his wife, Gullan M., members of the Massachusetts General Hospital Corporation, gave $15 million to erect the structure. Since then, Mr. Wellman pledged an additional $1.7 million to complete the Wellman Laboratories, including the laser lab, in the new building.



Patrick Mock, an engineer in the Wellman Resea from a tunable dye laser transmitted via fiberopti

With an argon laser already available, Dr. Parrish's group has also acquired excimer, tunable dye, and ruby lasers with the Wellman gifts. Plans call for employing alone or with drugs eight different kinds of lasers to study the effects of laser light on tissue.

One exciting aspect of the research in this new field called photomedicine concerns the ruby laser, which has a pulse that varies in duration from 10 millionths of a second to a billionth of a second.

Dr. Parrish plans to adapt the ruby laser to a so-called Nd:YAG laser capability. Nd:YAG stands for the element neodymium coupled with yttrium aluminum garnet, an artificial diamond.

MGH neurosurgeons visualize the possibility of using the YAG laser in brain surgery because the YAG beam is absorbed by material that is red, and thus can serve as an excellent tool for coagulating blood. YAG would complement the cutting or vaporizing power of the CO_2 laser.

YAG would also expand the treatment measures that gastrointestinal specialists could take through the endoscope, a special lighted instrument extended through the mouth into the abdomen.

"With the laser you can stop GI bleeding from an ulcer in the stomach or duodenum," said Dr. James M. Richter of the GI Unit. "We can do the same using electric cautery, but that requires touching the intestinal tissue.

Animal Research

(Concluded from Page 3)

but they teach us adaptive techniques. They teach us how to live optimally in difficult ecologic circumstances," said Dr. Zapol, who is also an Associate Professor of Anesthesia at Harvard Medical School. "For example, Antarctic Weddell seals can hold their breath for 70 minutes to exploit a food source deep under the ice shelf.

"By learning how a seal manages to hold its breath so long, you can then try to figure out what man could do when faced with long periods without breathing, say with the induction of anesthesia. It may be advantageous to be able to induce such a complex diving reflex in man, because that is what the seal employs. We may thus learn adaptive strategies for use in man." ■

boratories, demonstrates a pulse of light

Since an endoscope allows tunnel vision but really no depth perception, control becomes an important issue. The laser is easier to use, and most likely safer."

YAG also offers hope of extending the survival of patients suffering from cancer of the esophagus.

"The tumor grows and concentrically narrows the esophagus so that it becomes increasingly difficult for the patient to swallow," Dr. Richter said in describing the disease. "Irradiation can treat this but usually produces scarring and as a result leaves a narrowed esophagus. Preliminary European studies suggest that the YAG can effectively attack the tumor through the endoscope. With three or four treatments, the laser beam can 'chisel' a channel through the food pipe."

The tumor almost always recurs, however. Despite the laser treatments, the patient likely will die in two years' time. "Without the treatments, many patients will succumb in six months from malnutrition because they're unable to eat," said Dr. Richter. "So the laser buys time for the patient, and although not cured he or she can live the remaining days normally."

Like the YAG laser, the argon laser can "weld" but is less powerful. Argon is used to treat a number of eye ailments, including glaucoma, and to remove port wine stains, a form of birthmark that occurs when spaces in skin fill with blood.

Dr. Parrish and his colleagues use the excimer laser to determine what effects the short pulse of this ultraviolet wavelength instrument have on skin cells that contain the pigment melanin.

Development of the tunable dye laser added an important dimension to existing medical laser technology because this laser can be tuned to a desired wavelength by simply using prisms and changing the type of fluorescent dye involved. The pulse in the dye laser is also shorter than in many other lasers.

"Lasers are presently underutilized in medicine," said Dr. Parrish, who is also Associate Professor of Dermatology at Harvard Medical School. "A better understanding of the optical properties of certain tissue as well as the amount of light which reaches it, and a knowledge of the collective properties of lasers — not just their brightness — would allow us to describe a new generation of laser applications which will do more than simply destroy tissue by heat."

Dr. Parrish also predicted that the future will see increased control over the structures being treated. His group is studying ways of directing substances, either immunologic or chemical, to predetermined laser targets so that they will absorb energy at the desired wavelength. The chosen wavelength "would affect the target and no other tissue." ■

Anemia: A Warning by the Blood

Was he working too hard? Was he overly concerned about personal matters? Whatever the reason, George B., a successful Boston businessman, no longer felt up to par. Once highly ambitious and energetic, he now found himself listless and easily fatigued.

While undergoing a routine company-sponsored physical examination, George dutifully reported his lack of pep, shortness of breath, and general lassitude. Tests that followed helped to save his life.

He learned initially that he was suffering from a deficiency of iron in his blood. In a man or postmenopausal woman, this commonly means an unnatural blood loss from the body.

George conceded that his hemorrhoids had been "acting up," but the doctor, suspecting a more serious problem, ordered more extensive tests.

The result was discovery of a cancer in the colon, part of the large intestine. Detected at an early stage, the entire cancer was removed surgically, and the patient soon regained his former good health.

Iron deficiency is one of the most common of a long list of blood conditions which fall under the heading of anemia. Doctors emphasize that anemia generally is not a disease but a symptom of some other underlying disorder.

"The bone marrow is the body's blood-producing factory," said Dr. Leonard Ellman, Director of the Hematology Laboratories at the MGH. "Anemia results when bone marrow production of red cells be-

(Continued on Page 6)

With Dr. Leonard Ellman looking on (left), Herbert Beard, Assistant Chief Technician in the Hematology Laboratory, processes a sample of whole blood through an automated blood cell counting system. A laser beam helps to detect any cell irregularities.

The Blood Reuses Much of Its Iron

(Continued from Page 5)

comes suppressed for some reason or when cells are lost or destroyed faster than the marrow can replace them."

Physicians diagnose anemia through laboratory testing of three blood factors: (1) the hematocrit, the percentage of the blood's liquid composed of the red cells, (2) the hemoglobin, the molecule which transports iron and oxygen in the red cells, and (3) the red cell count.

Even these tests may prove inconclusive, however, since the definition of what reading constitutes anemia has long been controversial.

Dr. William S. Beck, who directs the MGH Hematology Research Laboratories, explained that the altitude at which a person resides can affect the blood count.

"When you live at a high altitude, the lower level of oxygen causes a hormone [erythropoietin] to increase the red cells," he said.

"I know an attorney who lives in LaPaz, Bolivia, which is 14,000 feet high. He walks around with a hematocrit of about 55 percent, 13 percent higher than what is generally considered normal.

"If he became anemic and his count dropped to something like 45, some physician, unaware of the circumstances, might think he was perfectly well."

Dr. Beck also said that some time ago pregnant women were always thought to have anemia because their red cell count appeared to fall.

"Someone then discovered that the number of red cells didn't change," he said. "The volume of plasma in the blood increased. With the cells suspended in this larger volume, a lower cell count resulted."

The body uses about 25 milligrams of iron each day, but as the red cells break down, the blood recaptures most of the used iron and recycles it. The body actually needs only about 1 milligram a day from the diet, although menstruating women probably require 2 to 4 milligrams.

Dr. Ellman said it is relatively uncommon for people not to get sufficient iron in their diet. Red meat and certain types of leafy vegetables, such as spinach, are major sources for the mineral.

The doctor cautioned that a woman who experiences menstrual blood loss and is also a very strict vegetarian could over time deplete her body of iron stores. During pregnancy, a considerable amount of iron transfers to the fetus. Pregnant women therefore usually take iron supplement pills. And some blood donors give so frequently they also need such pills to avoid anemia.

Profound iron deficiency anemia can lead to heart failure. When the red cell count falls to very low levels, the heart must work extra hard to compensate, circulating blood more rapidly to nourish cells with whatever iron remains. Older individuals might not have the reserve capacity.

In addition to iron, healthy blood requires other nutrients, such as folic acid and vitamin B_{12}.

Folic acid (*MGH News,* May 1977) plays a leading role in the bone marrow's production of red cells. A deficiency of this vitamin first becomes apparent with the development of a type of anemia called megaloblastic anemia. Then the blood's white cells, which fight infection, and platelets, important in clotting, diminish.

Folic acid also promotes the production of DNA (deoxyribonucleic acid) which is the chief chemical component of genes, the basic units of heredity. Methotrexate, a drug used effectively in the treatment of leukemia and other cancers, interferes with folate activity and indirectly produces anemia. Dr. Beck is trying to devise ways of making methotrexate even more effective.

A shortage of vitamin B_{12}, leading to another form of anemia (pernicious anemia), also adversely affects the manufacture of DNA. Bone marrow cells reflect lack of DNA by making fewer red cells.

In 1934, Drs. George R. Minot, William P. Murphy, and George H. Whipple shared the Nobel Prize in Medicine for their discovery that liver in the diet can relieve pernicious anemia. In his Nobel lecture, Dr. Minot said "the idea that something in food might be of advantage to patients with pernicious anemia was in my mind in 1912 when I was a House Officer at the Massachusetts General Hospital."

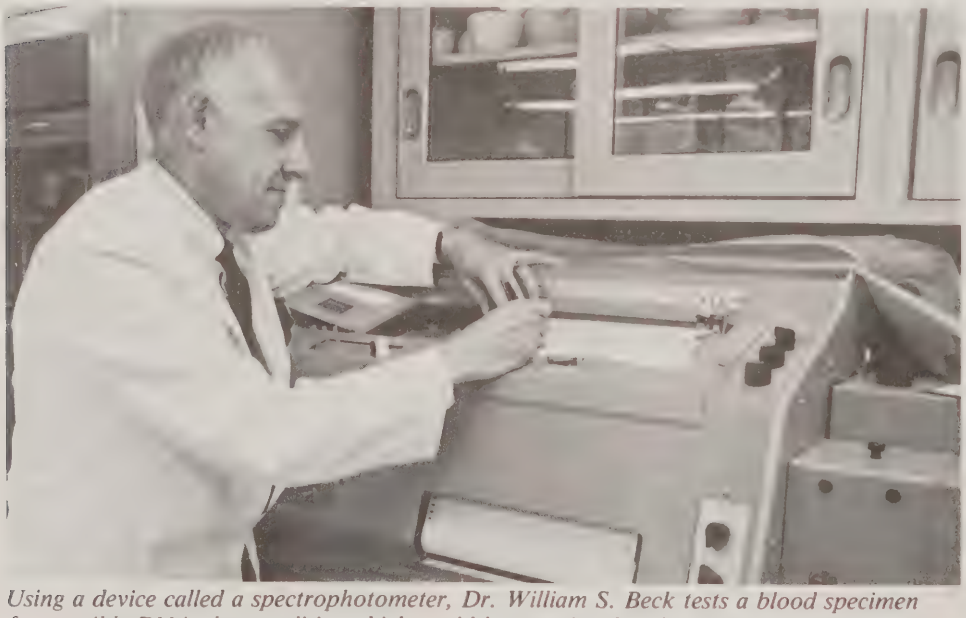
It was not until the late 1940s that vitamin B_{12} in liver was shown to be the ingredient which counteracted the anemia.

Dr. Beck, who is Professor of Medicine at Harvard Medical School, heads a study to learn more about the role in the body of vitamin B_{12}. He has also been instrumental in improving ways to measure the vitamin in blood.

High on the list of serious anemias are two conditions caused by genetic abnormalities: sickle cell anemia and thalassemia.

Sickle cell anemia (*MGH News,* November 1973) strikes one in every 400 black Americans, and death usually occurs by age 40. When exposed to low oxygen levels in the blood, the red cells assume a sickle, or crescent, shape which impairs the oxygen-carrying capacity of the cells.

Thalassemia, which also impairs the oxygen-carrying hemoglobin, principally affects individuals of Mediterranean ancestry. If a person inherits a single gene for thalassemia, the body can compensate for the resulting anemia, but when a gene is inherited from both parents, the anemia becomes severe, blood transfusions are required regularly, and a shortening of the life span occurs.



Using a device called a spectrophotometer, Dr. William S. Beck tests a blood specimen for possible DNA abnormalities which could be associated with a type of anemia (megaloblastic anemia).

Detecting Artistic Talent in a Young Child

At left, a drawing of a horse by a typical five-year-old, and at right Pablo Picasso's Study for Guernica

When a preschooler draws, the freely developed shapes and designs that result may sometimes resemble the work of contemporary abstract artists.

Pablo Picasso once said, "I used to paint like Raphael, but it's taken me a lifetime to learn to draw like a child."

Looking at a multitude of pictures by young children, how can a knowledgeable observer discern the precious few examples which reflect talent?

"I look for a sensitivity in children to important aesthetic properties in art and whether the youngsters can produce these qualities," said Ellen Winner, Ph.D., Assistant Professor of Psychology at Boston College and Research Associate at Project Zero, Harvard Graduate School of Education. Project Zero is involved in studies of artistic and symbolic development.

Author of *Invented Worlds: The Psychology of the Arts,* published last year by Harvard University Press, Dr. Winner spoke at an MGH medical meeting (Psychiatric Grand Rounds) on creativity in children.

"The properties which set something apart as art from nonart are style, expressivity, and composition," she said.

In a line drawing, for example, the texture, rhythm, color, and variation of thickness of each line provide style. Expressivity refers to moods that an artist instills in his work. Composition is the structural organization of the parts that make up the finished product.

"Every aspect of a work of art counts and is meant to be noted," Dr. Winner emphasized. "Take a zigzag line. If I say it is an electrocardiogram, then the only important things to notice are how high up the peaks are and how low the dips are. If, however, I tell you that this same line is an outline of a mountain from a Japanese pen and ink landscape drawing, then you have to focus on a lot more. All of its properties become important."

Dr. Winner, who also serves as a consultant to the Dallas Museum of Art and the Toledo Museum of Art, described the work of the young, gifted child (aged 3 to 8) as more like that of the adult abstract artist than the older child (aged 9 to 12) for one important reason: The younger one has not yet learned the rules of realism.

"The time for mastering rules in our culture is during the school years," she said. "This is when youngsters enter the 'literal' stage in drawing. They seem possessed by one goal, to draw something exactly the way it looks.

"The usual finding in developmental psychology is that things get bigger and better with age, but here a kind of aesthetic quality appears lost with age."

For the gifted child who continues to nourish his artistic talents, the loss is only temporary. As time goes by, he may quickly recultivate his sense of originality and free expression. Thus, the developmental force in drawing may follow a U-shaped curve.

In her MGH talk, Dr. Winner spoke of visiting an art exhibit in Israel. The

(Concluded on Page 8)

Dr. Ellman, who is also Associate Professsor of Medicine at Harvard Medical School, said a drug has been found which may help patients with either sickle cell anemia or thalassemia.

"The drug, called 'm-Amsa,' is said to stimulate the production of fetal hemoglobin in adult red blood cells," Dr. Ellman said. "Normally, fetal hemoglobin disappears by three months of age, but the drug makes it reappear."

Physicians frequently encounter anemia in patients hospitalized with some chronic inflammatory condition, such as a urinary infection, ulcerative colitis, hepatitis, or a form of cancer. The inflammation seems to suppress the bone marrow. The anemia vanishes when the inflammation clears up.

When the bone marrow has been reduced in quantity or has been infiltrated by cancerous cells, such as leukemia, life-threatening aplastic anemia results (*MGH News,* September–October 1973). The bone marrow fails to produce red cells, white cells, or platelets.

Over the years, bone marrow transplants, involving compatible siblings, have proved increasingly successful. In addition, Dr. Ellman and Dr. A. Benedict Cosimi, MGH Chief of Clinical Transplantation Surgery, have helped to develop a serum for use against a certain form of aplastic anemia.

"Many instances of aplastic anemia appear to stem from autoimmune diseases in which white cells [lymphocytes] from the body's own thymus gland attack the bone marrow," Dr. Ellman said. "By using an antibody prepared in horses against the T-lymphocytes, we and others have found that approximately half of patients with autoimmune-caused aplastic anemia can develop a permanent remission." ■

Address Correction Requested

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Handicapped Child Impresses Art Critics

(Concluded from Page 7)

work of well-known contemporary artists was lined up next to samples of what they had drawn as children.

The gifted children did not seem as rigid in their artistry during the literal stage as other youngsters would be, and the literal stage passed more quickly for the more talented.

Dr. Winner cautioned that although a child's drawing might look like the work of a master, the child might not be in control of the effects he is producing.

"Suppose you see a drawing full of very bright colors," she explained. "Someone might comment, 'Look at how well the child expresses gaiety.' But perhaps the colors used were the only ones available to the youngster.

"Or the child might execute very thick brush strokes which you might consider very interesting. It could turn out that the child had no option on the type of brush to paint with."

In underscoring how easy it is to misinterpret the work of a child, Dr. Winner told of a psychiatrist who sought to analyze a youngster's personality from his drawings. The doctor noticed that the pictures showed little people at the bottom of the work. Did the child have an inferiority complex? It turned out that in painting the figures the youngster used an easel, and their location on the picture represented the height that he could reach.

In art as in most creative aspects of life, prodigies appear. Dr. Winner mentioned an English child named Nadia who was practically mute and who performed very poorly on intelligence tests. At the age of 6½, she was formally diagnosed as suffering from autism, a disorder characterized by inability to develop language, social, or interpersonal skills (*MGH News,* April 1981).

If one gave Nadia a crayon to draw with, she would hold it clumsily, rub it on a piece of paper, and produce a scribble that a 2-year-old might make. Give her a ball-point pen, however, and she could create a masterpiece!

Nadia, who began to draw at 3½, did not look at a model and then proceed to copy it. She preferred to rely on her memory and reproduce something she had seen much earlier. The result of her effort was usually incredible.

Since the typical child learning to draw starts out by scribbling, then moves on to very simple schematic, geometric forms, such as circles for heads, and later achieves a stereotyped realism, Nadia's early, almost photographic renditions were very atypical.

What gave rise to Nadia's unique prowess is anybody's guess. Dr. Winner suggested that perhaps the little girl possessed some innate neurological proclivity for visual perception and motor skills. In addition, the absence of competition from other skills, e.g., language or logical reasoning, may have actually enabled her to hone her single talent to the degree whereby she could achieve immediately what other artists need years to work out.

The psychologist said the typical child and the gifted, nonautistic youngster go through parallel stages in drawing development, but the talented student travels the route much more quickly. On the other hand, the autistic child with a genius for the visual arts probably follows an entirely different path.

"Children like Nadia may share with an adult artist a special sensitivity to visual contours as well as visual memory," Dr. Winner said, "but the autistic child prodigy appears to have no choice but to draw in an optically realistic style. In contrast, the pure artist is free to choose whether to draw realistically or not." ■

Drawing (left) by an autistic child, Nadia, at age 5½ is shown alongside Leonardo da Vinci's Study for the Sforza Monument.

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 42 No. 6 September, 1983

Drug Studies Fuel Drive to Curb Memory Disorder

Inhibitions Plague Many Working Women

Some 200 analysts were once asked in a survey whether they would accept an invitation to speak publicly.

Of 150 men in the group, 20 percent said no. Among the 50 women analysts, 50 percent said they would refuse.

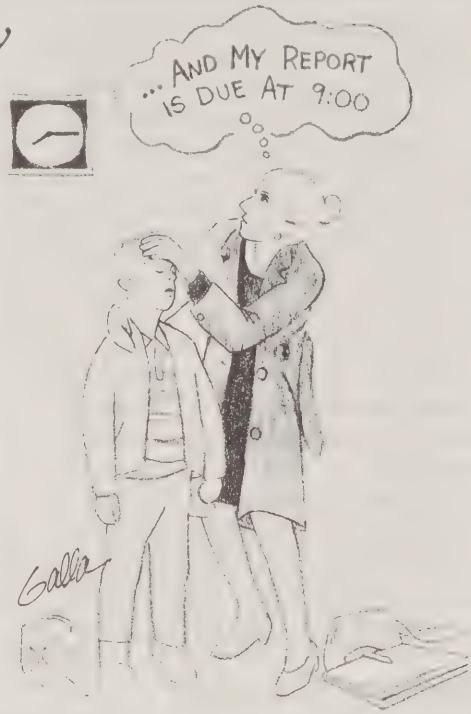
Among academically proficient boys and girls, another survey found the brighter the boy the better he expected to do in the future, and the more he attributed his high scores to his competence. In contrast, the brighter the girl the less likely she was to regard her good work as a reflection of her own capability, and she did not expect to do better in the future.

Irene P. Stiver, Ph.D., director of psychology at The Massachusetts General Hospital Corporation's McLean (Psychiatric) Hospital in Belmont, Mass., cited the two surveys to underscore inhibitions that hamper females in their competition with males.

Speaking at a medical gathering (Psychiatric Grand Rounds) at the MGH, Dr. Stiver focused on women in the workplace:

"We know that for men work supports their identities as men and is a major force for enhancing their self-esteem. Successful men are seen as more masculine than the less successful. Men who move ahead are talked about with value-laden words such as self-initiators, go-getters, etc.

"When women move into the work arena, however, they immediately experience a conflict between being successful and their identities as women. With advancement they may be described in pejorative terms such as 'too pushy,' 'too aggressive,' and often 'unfeminine.'"



Finding time to fulfill both family and job responsibilities can be stressful.

While men believe work problems legitimize their visits to a psychiatrist or psychologist, Dr. Stiver said that women more often seek consultations on matters dealing with personal relationships. Only as treatment progresses does it become evident that work is also an issue.

Data in the psychiatric literature do, in fact, seem to indicate that women as a group experience more stress in work situations than men.

On listening to women talk about their work experiences, Dr. Stiver repeatedly finds them plagued with enormous self-doubt and a conviction that they must play down the degree of

(Continued on Page 2)

In 1907 when Dr. Alois Alzheimer, a German physician, first described the brain disease that bears his name, most colleagues considered the condition to be a normal part of aging.

Although Dr. Alzheimer pointed to an abnormal accumulation of fibrous material within nerve cells as a unique characteristic of the disease, no one could offer a way to deal with the problem. Paradoxically, it sometimes arose in patients as young as 45.

A status quo persisted until recent years when three independent laboratories in England concentrated new interest in Alzheimer's. The work has led to the development of drugs which may help combat the disease. These drugs are undergoing trials at the MGH and other medical centers at home and abroad. In some instances the very early results have been described as encouraging.

"The researchers reported that in

(Continued on Page 4)

Interpreting the Actions Of Alzheimer's Patients

"Aside from the stress of dealing with somebody who needs close watching and care, we think the biggest problem faced by the family of an Alzheimer's disease patient is how to interpret the person's behavior."

Marilyn Albert, Ph.D., a neuropsychologist, and Dr. Michael A. Jenike, head of inpatient psychiatry at the MGH, codirect the hospital's Geriatric Psychiatry Evaluation Team.

They spoke from long experience with Alzheimer's patients who comprise 90 percent of the people examined by the team.

"Families often have difficulties be-

(Continued on Page 6)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114 Telephone (617) 726-2206

Martin S. Bander — *Editor*
Myron H. Daniels — *Assistant Editor*
Doris G. Schreckengaust — *Copyreader*

EDITORIAL BOARD

J. Robert Buchanan, MD — *General Director*
Kurt J. Isselbacher, MD — *Research, Medicine*
Paul S. Russell, MD — *Surgery*
Ronald A. Malt, MD — *Surgery*
Roger H. Sweet, MD — *Utilization*
Stanley Bennett — *Photography*
Robert J. Galla — *Designer*

EDITORIALS:

Reducing the Risk of Cancer

Suppose there were several vaccines, each of which could significantly reduce your risk of a major type of cancer. Let's assume these vaccines were risk free. Finally let's suppose that they actually reduced your expenses or at least added no extra cost. Would you get these vaccines?

There obviously are none as yet. But there do exist some nonvaccines that seem to offer the very advantages described. The most obvious is nonsmoking. The person who gives up smoking saves money directly. In the process the former smoker decimates the risk of the most common cancer, carcinoma of the lung. Eliminating cigarettes is risk free. And, in the absence of smoking, other deadly forms of cancer also become far less prevalent. By remaining cancer free and more healthy in general, the nonsmoker also saves thousands of dollars in medical costs.

In addition a page 6 article in this issue describes ways that seem likely to reduce cancer's toll by avoiding certain foods. Studies are continuing to add to the list of dietary items that cause cancer, at least in animals. Research is also delving into foods and vitamins that might prove to have a protective effect against certain cancers.

On page 7 of this issue appear a few guidelines of nutritional "dos" and "don'ts." The key word is "guidelines." If medicine is an art rather than a science, then the current knowledge of cancer nutrition can be equated to the primitive drawings in the caves of Altamira in Northern Spain. Until many more facts appear, moderation rather than fad diets is called for.

Inhibitions of the Working Woman

A page 1 article in this issue describes some of the psychological problems faced by women entering the working world. It is unfortunate that they bring to their work inhibitions and frustrations that arise from conditioning to their traditional role in history. Being a pioneer was never easy. For today's working women this leap into destiny confronts centuries of stereotypes about roles and about biological limitations. Despite the protestations of the most ardent feminists, physical endowments do provide men with advantages of strength. Training and conditioning may narrow but not eliminate these structural assets. Hormonal infusions would make a difference as well as carry along some attendant risks and ethical considerations.

Such factors, however, pale in the realization that few jobs these days demand strength. And with the advent of automation the future will see a continued dwindling of those jobs. On the contrary women are well equipped for the vast number of positions that are opening to them. As they achieve success, inhibitions and feelings of inferiority will diminish. Once men begin to accept women as colleagues in formerly unaccustomed places, men too will overcome the prejudices that derive largely from fears of the new competition.

Women Often Doubt Competence on Job

(Continued from Page 1)

their effectiveness and competence.

"This I find very marked and pervasive," she said. "They minimize their intellectual worth and their inner ambitions. When on occasion their good intelligence does overcome discretion and they speak up, ruminations follow. 'Did I say too much? Did I say too little? Was I too aggressive? Did I make a fool of myself?'

"Women tend to attribute their successes to chance events, being at the right place at the right time."

In her MGH lecture, Dr. Stiver mentioned a *New York Times* article in which television newswoman Betty Rollin discussed her own seemingly perpetual self-doubts.

Despite years of success, Miss Rollin wrote of "fear, sometimes terror, rising like steam with the onset of each new assignment, whether on camera or paper." She added, "Not until a task is done, do I ever believe that it can be done."

She was sure that men also experience self-doubts, but she read somewhere that they are repressed. Dr. Stiver recounted the following dialogue between Miss Rollin and a young male colleague:

"'When you're on a story, do you ever think that it's not going to work out?' Miss Rollin asked.

'Sure,' he replied, not sounding sure.

'When it doesn't work out, do you usually think that it's your fault?'

'No,' he said, sounding sure.

'Suppose that it is your fault. Does it make you feel terrible?'

'Naw.'

'Why not?'

'Aren't I entitled to make a mistake once in a while?'"

Dr. Stiver said Miss Rollin does not feel so entitled, and the psychologist added, "I think women in general do not."

She said women are very aware of their tendency to belittle themselves. "They joke about it," she declared, "but they really do believe they are fooling people, that they don't know as much as other people know, or think

---

Drawings: Pages 1, 3, MGH Medical Art

Photographs: Pages 4, 5 (lower), 6, 8, Myron Daniels; p. 5 (upper), courtesy of Dr. Dennis J. Selkoe, McLean Hospital; p. 7, courtesy of United States Department of Agriculture

they know.

"They therefore feel very inadequate and unable to function on their own, which often keeps them tied to a subordinate, dependent position where they work."

What induces women to hold onto such views, to resist change? Recent writings on women's issues have stressed how much women need to feel related and connected to another individual as a crucial aspect of their identity.

"I do think women have learned that assuming a dependent position is the major mode available to establish a connection, a relationship, particularly with men," Dr. Stiver said.

For many working women who simultaneously hold significant household responsibilities, a very precarious balance exists.

"Family tasks involve more than just the sum of the hours needed to execute those tasks," the McLean Hospital specialist declared. "If a woman's real identity is a relational one, then we have to recognize the intense emotional bonding with people at home and the energy that calls for. The wrenching away from home to work takes much more of a toll on women, I think, than on men."

Because of the delicate balance that exists between home and work, women strive to avoid situations on the job that might stir up more anxiety than they can tolerate. The literature states that when opportunities for advancement arise, women often see them, not as welcome challenges, but rather as burdensome obligations.

"I think, too, that the kind of self-doubts they have makes it harder for women to take risks," Dr. Stiver declared. "If new opportunities arise, they may be more timid and cautious because they don't have confidence in themselves. But I think one should also note how ambivalent women are about this because if they get passed over or opportunities are not available, they do feel quite resentful and bitter."

Instead of viewing them as opportunities, women sometimes regard the obligations of advancement as unwelcome burdens.

Dr. Stiver said that women are very concerned about behaving professionally at work. They even try to stifle certain feminine characteristics, such as expressing compassion, she stated, lest a domino effect result with all of their feelings being laid bare.

In particular, Dr. Stiver adds, women regard crying as the worst kind of unprofessional display. Some women become so preoccupied with the thought of this that at meetings they will not speak up on highly charged issues for fear of becoming visibly upset. The alternative is to withdraw into the background.

"In therapy, I try to validate for women the intrinsic conflict between success as defined in our culture and the qualities women value for themselves," Dr. Stiver said.

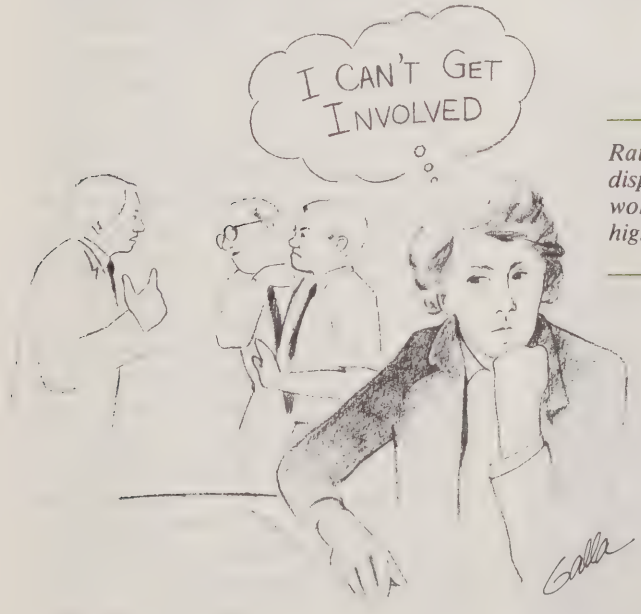
"I also help them see how much they have internalized certain assumptions, attitudes, stereotypes of what is better, worse, good, bad, valued, not valued, often based on some masculine model of work and success which may often be more destructive than constructive, and sometimes not humane.

"Women do not have to adopt the values of a culture if these include lack of concern for others or advancement at the expense of others."

Dr. Stiver emphasized that it is important for women to affirm their more person-directed and empathic qualities. If these interfere with attaining higher status and more power, she said, the basic problem is not the woman's.

And women must be encouraged to pursue their career interests and realize their intellectual and creative potential. If this is perceived as selfish, Dr. Stiver said, the basic problem again is not the woman's:

"The hope is that women can learn to experience these conflicting attributes as less alien to their sense of self as both women and as competent, effective human beings." ■



Rather than risk an unprofessional display of emotion, many working women avoid confrontations on highly charged issues.

Alzheimer's Patients Deficient in Vital Brain Protein

(Continued from Page 1)

addition to anatomical and pathological changes that had been known, the brains of Alzheimer's disease patients were found at autopsy to have a significantly lower level of an important neurochemical," said Dr. John H. Growdon, an MGH neurologist and director of the hospital's Memory Disorders Unit.

Dr. Growdon established the MGH unit one year ago, and now it has become an important and official area for treating and delving into the mysteries of Alzheimer's disease.

The deficiency was in a brain enzyme (choline acetyltransferase), a protein which stimulates the production of acetylcholine, a chemical compound active in the transmission of nerve impulses that are believed to underlie learning and memory.

Investigators reasoned that if a deficient chemical process contributed to Alzheimer's, perhaps they could develop drugs to improve acetylcholine function and thereby lessen the illness symptoms such as memory loss, language difficulties, trouble with visual perception, personality changes, and behavioral disorders.

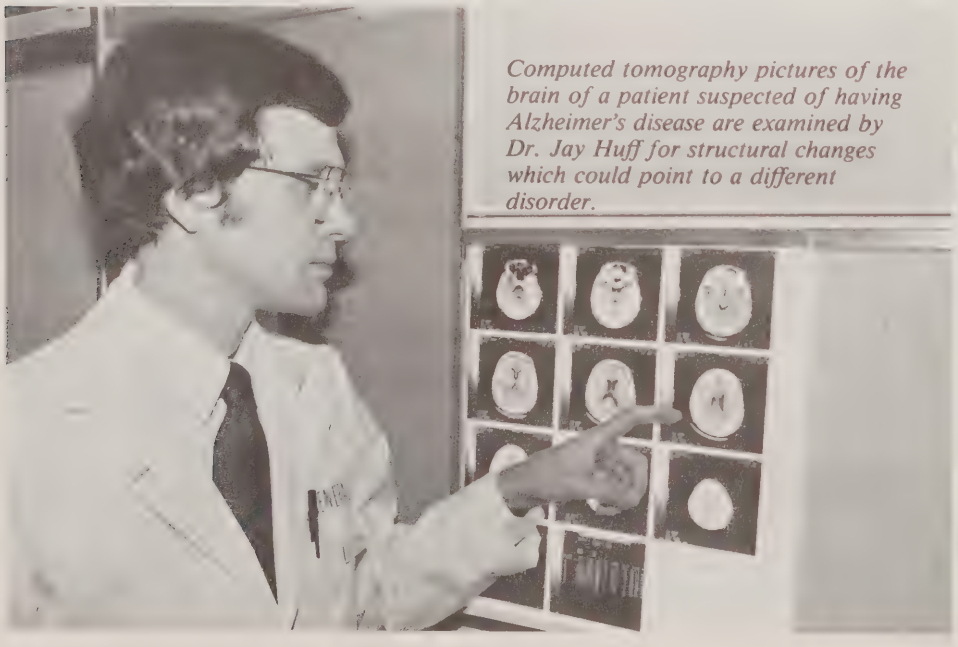
An analogy can be found in the use of the drug L-Dopa to treat another incurable problem, Parkinson's disease, which is a nervous system disorder (*MGH News,* May 1976). L-Dopa makes up for the brain's deficiency of dopamine, another substance involved in transmitting nerve signals.

Using a procedure called high pressure liquid chromatography, Dr. John Growdon tests a sample of a patient's spinal fluid for possible evidence of abnormalities which might occur in Alzheimer's disease.

Since studies on Alzheimer's brought a resurgence of hope for such patients, concerned groups have pleaded in Washington for stepped-up research funding. Appearing before one congressional committee, Princess Yasmin Aga Khan said that the illness had reduced her mother, Rita Hayworth, to a "state of utter helplessness."

Cognizant that between one and two million Americans over 65 have the condition, the United States Senate adopted a resolution to designate November as National Alzheimer's Disease Month.

Seventy percent of the patients seen in Dr. Growdon's Memory Disorders Unit since its founding were diagnosed as having Alzheimer's. Their mean age is in the 60s, but several patients developed the first signs of their condition in their 40s.



Computed tomography pictures of the brain of a patient suspected of having Alzheimer's disease are examined by Dr. Jay Huff for structural changes which could point to a different disorder.

Of other patients in the unit, about 10 percent suffer from memory loss associated with severe depression. The remainder have neurological problems attributable to multiple strokes, brain tumors, concussions, multiple head injuries (sometimes called the "punch-drunk" syndrome), or a condition in which fluid-filled chambers in the brain enlarge and press upon surrounding tissue (normal pressure hydrocephalus).

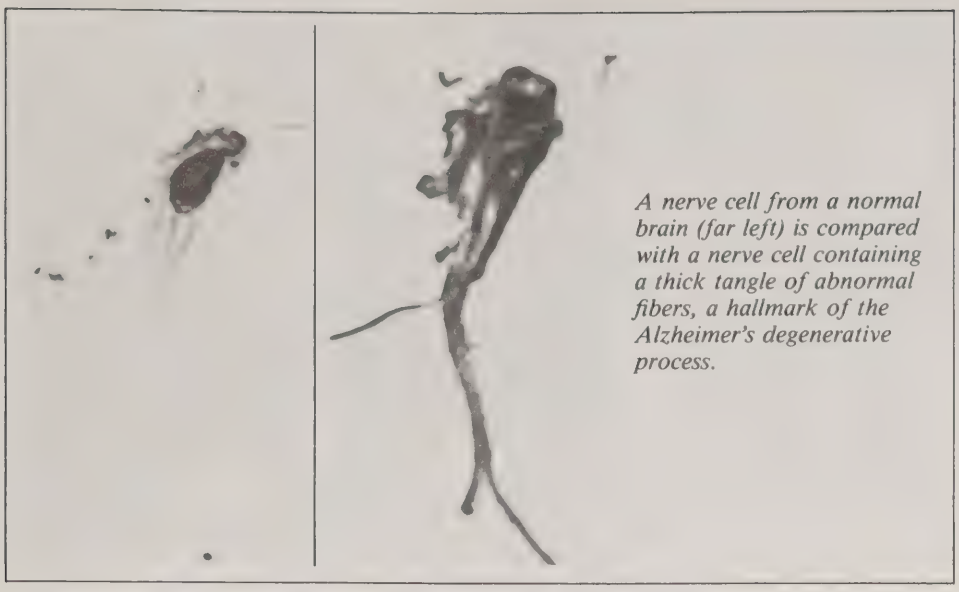
"Some of the conditions are treatable; others are preventable in terms of further progression; and some, like Alzheimer's disease, still need to be defined," Dr. Growdon said.

The unit thus was established with three goals: to provide an accurate diagnosis for patients with memory problems, to treat the symptoms whenever possible as they emerge, and to conduct research.

Since no animal model exists for the study of Alzheimer's, specialists must turn to groups of patients such as those in the Memory Disorders Unit to learn more about the disease and how best to combat it.

The unit meets every Monday afternoon between 1 and 5 in Suite 735 of the MGH's Ambulatory Care Center. To diagnose Alzheimer's disease, physicians must eliminate all other possibilities.

After obtaining the history of a pa-



A nerve cell from a normal brain (far left) is compared with a nerve cell containing a thick tangle of abnormal fibers, a hallmark of the Alzheimer's degenerative process.

tient, Dr. Growdon or a neurologist colleague, Dr. Jay Huff, first examines the individual and schedules needed diagnostic tests. These may include a CT (computed tomography) scan to detect any anatomical abnormalities, or an EEG (electroencephalogram), which records the electrical activity of the brain.

Investigators reasoned that if a deficient chemical process contributed to Alzheimer's, perhaps drugs could lessen the illness symptoms.

Dr. George B. Murray, an MGH psychiatrist, often conducts a psychiatric interview to supplement the neurological studies before members of the unit draw up a plan of medical care. Collaborating on the plan are a nurse, social worker, and, when necessary, a speech-language pathologist.

"Identifying the Alzheimer's patient can be a complicated procedure," said Dr. Growdon, who is also Associate Professor of Neurology at Harvard Medical School.

"Many Alzheimer's patients have large ventricles [chambers] in their brain, and on a CT scan these can mimic the large ventricles of the patient who has treatable hydrocephalus. Many Alzheimer's patients also are severely depressed and require antidepressant medications."

Dr. Growdon has long been active in Alzheimer's research and was in the forefront of efforts to learn more about the body's production of acetylcholine. In conjunction with colleagues at the Massachusetts Institute of Technology, Drs. Richard J. Wurtman and Suzanne Corkin, he has organized three international meetings devoted to the treatment of Alzheimer's disease.

Dr. Growdon, together with Drs. Wurtman and Corkin, discovered that large amounts of lecithin, the dietary source of choline, could play an important role in the brain's production of acetylcholine and might therefore be a useful way to treat Alzheimer's.

Lecithin is found in such foods as egg yolk, soy bean products, fish, liver, and meats.

Dr. Growdon and other investigators gave purified lecithin to a number of Alzheimer's patients for one month without noting any beneficial effects. However, a researcher in London, Dr. Raymond Levy, reported positive results when he continued the treatment for six months.

Writing in the British journal *Lancet,* he said that on the basis of psychological test results patients who took lecithin daily did not suffer further progression of the disease while those individuals given only nonmedicated pills (placebos) deteriorated at an expected rate.

Currently, Dr. Growdon directs several Alzheimer's drug trials at the MGH. One involves the use of physostigmine in conjunction with lecithin.

"Physostigmine, which has to be given every two hours, blocks the degradation of acetylcholine while lecithin increases the production of acetylcholine," the doctor explained. "So we're cranking up acetylcholine transmission by two different mechanisms."

The MGH is also trying with lecithin, a drug developed as a "cerebral activator" and marketed only in Europe. Preliminary results with piracetam have been promising. A derivative, aniracetam, also is undergoing study.

On another research front, physicians stress the importance of autopsies on deceased Alzheimer's patients and the availability of brain tissue from such patients for laboratory study. Arrangements for donations can be made through Dr. Growdon at the MGH or by contacting Dr. Edward D. Bird or Dr. Dennis J. Selkoe at the Mailman Research Center at McLean Hospital, an MGH affiliate, in Belmont, Mass.

Aside from the considerable laboratory value obtained from examining brain tissue from an Alzheimer's victim, only through a pathological examination can the family of a patient be certain that the illness was indeed Alzheimer's disease. ■

Patients find lecithin more palatable as an ingredient in soup..

Alzheimer's Patients Want Understanding

(Continued from Page 1)

cause they misinterpret the behavior of Alzheimer's patients and in trying to help them may instead do them harm," Dr. Albert said. "That is why our evaluation team tries to not only provide the family with a diagnosis but also give guidance in the care of the patient."

Drs. Albert and Jenike told of a patient whose condition was pictured as very advanced: He could not feed himself. He sat and slept all day. He was getting lost in his own home.

It turned out that the patient, a philosophy professor, was one of a subgroup of Alzheimer's patients whose illness begins with dramatic visual spatial deficits. He knocked things over because he could not see them correctly. He became lost because he could no longer distinguish between right and left. Given literary material, he did not know where to begin reading on a page, and so fell asleep.

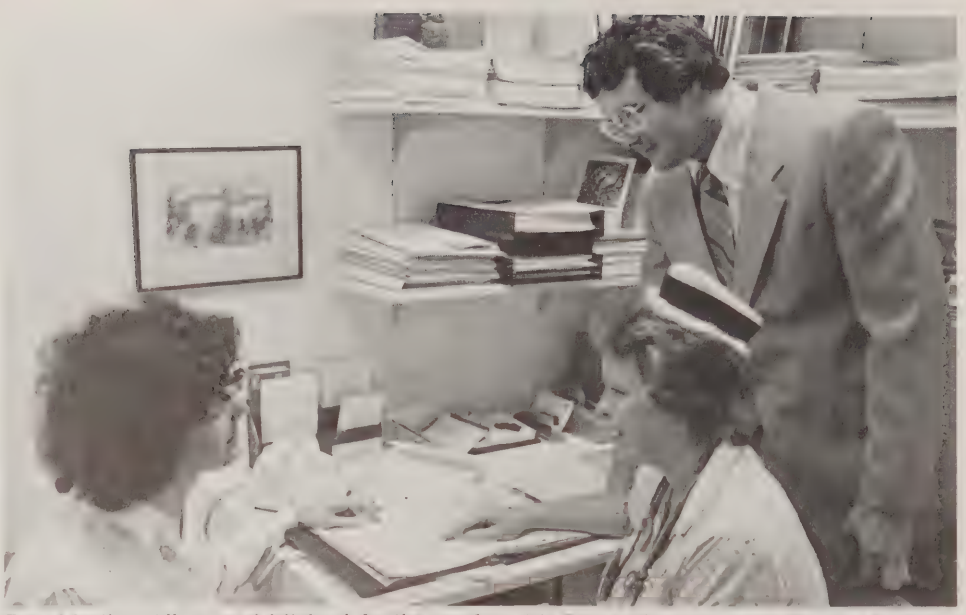
Because of the clear deterioration, the family tried to persuade the professor to give up conferring with his colleagues, a move which would have been unfortunate.

"He could still appreciate some of the knowledge he had gained in his youth and also carry on a reasonable conversation," Dr. Albert said. "Sitting and talking with fellow scholars about what he had learned years earlier helped to keep him functional and content."

Hoping to retard the progress of disease, relatives often test a patient repeatedly. "Now what did I tell you about this yesterday?" they ask.

"Many patients, perhaps as many as half, are fully aware of what is transpiring," Dr. Jenike said. "Questions like this make them feel incompetent and useless."

Sometimes, Alzheimer's disease aggravates family problems of long standing. The husband who has always been too demanding of his wife, for example, may find it difficult to adapt to the fact that, with Alzheimer's, she is not the same person. He may continue to criticize her, and she, in turn, will only feel worse about herself.



Drs. Marilyn Albert and Michael Jenike confer with Diane Sherman, a staff nurse in the MGH's General Clinical Research Center, on a patient being treated for a memory disorder.

As in the Memory Disorders Unit, patients of the Geriatric Psychiatry Evaluation Team first receive a neurological examination from Dr. John H. Growdon or one of his neurologist colleagues. Then Drs. Albert and Jenike plus a social worker and a speech pathologist meet with the patient and family.

Each session of the team, which meets Thursday afternoons in the Psychopharmacology Unit of the MGH's Ambulatory Care Center, may deal with only one patient.

"Our goal," said Dr. Albert, who is also Assistant Professor of Psychiatry and Neurology at Harvard Medical School, "is to determine the patient's impairments, how the family is relating to them, and how we can best help the family maximize the function of the patient within the particular setting."

For the first time in its 57-year history, the MGH's famed General Clinical Research Center, formerly known as Ward IV, is being used to study Alzheimer's patients. Drs. Albert and Jenike are assigning patients there for three-week stays while undergoing trials of a drug called physostigmine.

The Geriatric Psychiatry Evaluation Team also is one of only a handful of groups in the nation studying a drug, CI-911, designed to increase metabolic activity in the brain. During the next year the team hopes to study 50 patients in this outpatient program.

"A lot of people ask me, 'Don't you get depressed dealing with Alzheimer's disease patients all the time?' And I tell them I feel just the opposite," Dr. Jenike said. "I feel that we're really on the threshold of being able to understand and treat the disease. For that reason, it's a very exciting time." ■

How Dietary Habits May Block Cancer

For years researchers have probed substances in food to try to learn whether any cause cancer, which accounts for one of every five deaths in this country.

Because evidence pinpointing cancer-causing or cancer-promoting agents in the diet has been slow to accumulate, many investigators, including a team at the MGH, have approached the problem in another way.

In addition to trying to identify harmful foods that people eat, the researchers have begun searching for ingredients in food that may actually protect against cancer.

Studies indicate that two-thirds of all cancers stem from factors controllable by man. One-third of cancer patients can attribute their plight to what they ate or drank, another third to substances in the air they breathed.

Theoretically, therefore, by eliminating environmental hazards, such as the inhalation of tobacco smoke and other irritants, and by carefully modifying the diet to include only wholesome foods, one can dramatically reduce the chances of contracting cancer.

Some environmental threats already are well defined. The Surgeon General of the United States has described cigarette smoking as the leading cause of lung cancer, the most common cancer in western nations. It is also clear that excessive exposure to rays of the sun

can produce skin cancer.

With regard to the diet, however, studies have focused on a long list of food ingredients, such as artificial sweeteners, preservatives, saturated and unsaturated fats, alcohol, etc., but while interim reports have often tended to raise or lower suspicions, most of the studies are still ongoing. Thus the new tack.

In the MGH's Cox Cancer Center, Dr. Sigmund A. Weitzman is a member of a Hematology–Oncology Unit team studying whether certain factors, including nutritional ones, can lessen the harmful effects of chronic inflammation which contribute to the development of cancer.

"The inflammatory response produces things we call 'radicals' which can injure normal tissue," he said. "Some of the substances we are working with, such as the nutrients beta-carotene [a precursor of vitamin A], vitamins E and C, and selenium, may reduce the toxicity of these radicals.

"If so, by understanding the process better, we may find we can manipulate developments pharmacologically and hold down the genetic damage."

Dr. Thomas P. Stossel, Chief of the Hematology–Oncology Unit; Dr. Alan B. Weitberg, and Technician Marilyn Belmonte round out the study team.

The nutrients mentioned by Dr. Weitzman have demonstrated in other research that they may act to inhibit cancer, but the results have often proved to be little more than suggestive.

"There have been some animal experiments in which these nutrients appeared to prevent certain types of cancer from developing," the doctor said, "but these trials were conducted under highly controlled laboratory conditions. There is no proof that humans would react the same way."

Ample daily servings of fruits or vegetables containing vitamins A and C may help lower a risk of cancer.

He pointed out at the same time that if taken in excessive doses, both vitamin A and selenium, a metallic element, can be very toxic.

The danger of consuming too much vitamin A can be offset by substituting vegetables rich in beta-carotene, such as yellow and dark green vegetables. Although it converts to vitamin A, beta-carotene is stored in the body in a nontoxic form.

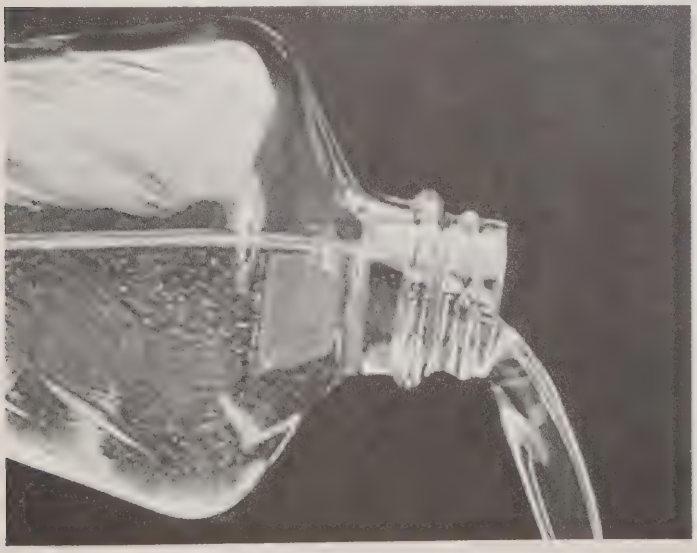
Studies some years ago on vitamin A and beta-carotene helped to spark the current drive to find possible cancer inhibitors in food. Researchers discovered that individuals who consumed liberal amounts of carotene-rich foods seemed to face a lower risk of certain cancers than other people.

Laboratory investigations of vitamin C (ascorbic acid) have indicated an association between this nutrient and a lower risk of cancer of the stomach and esophagus.

Abundant in citrus fruits and in many vegetables, vitamin C appears to prevent a cancer-causing chemical called nitrosamines from forming in the stomach following ingestion of foods to which manufacturers have added nitrates as a preservative.

To avoid the possibility of stomach

(Concluded on Page 8)



Diets high in fat may contribute to the development of certain cancers.

For Healthier Living

The Committee on Diet, Nutrition, and Cancer of the National Academy of Sciences has proposed that the following nutritional guidelines seem likely to reduce the risk of cancer:

- Reduce the intake of both saturated and unsaturated fats to approximately 30 percent of total calories. The typical American diet now contains about 40 percent fat.
- Include fruits, vegetables, and whole-grain cereal products in the daily diet, especially citrus fruits and carotene-rich (such as dark green lettuce) and cabbage-family vegetables.
- Avoid high-dose supplements of individual nutrients.
- Minimize consumption of cured, pickled, and smoked foods.
- Drink alcohol only in moderation.

The Academy committee said that despite much evidence concerning cancer and its relationship to certain dietary patterns and individual dietary components, "the data are not sufficient to quantitate the contribution of diet to the overall cancer risk or to determine the percent reduction in risk that might be achieved by dietary modifications." ■

Address Correction Requested

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Several Nutrients May Cut Cancer Risks

(Concluded from Page 7)

cancer, nutritionists advise against frequent consumption of spiced, pickled, or smoked foods.

Interestingly, in Japan where such foods are popular, the incidence of stomach cancer is high, but Japanese who emigrate to the United States and change to a western-style diet appear to face a much lower risk of this disease.

"Like ascorbic acid, vitamin E, found abundantly in vegetable oils and margarine, also seems to inhibit the formation of tumors," Dr. Weitzman said. "And there is limited evidence from animal studies that E also acts against tumor production by other chemicals. There is not enough information yet to form any definite conclusions about how this vitamin may affect cancer in humans."

The body needs selenium in minute quantities to protect tissue from damage by oxidation (*MGH News,* December 1978). Found in water and in all plants, selenium was once suspected of causing cancer because grazing animals sometimes became sick in areas of the nation's midwest, where the soil has heavy amounts of the element.

Further check, however, indicated that people living in regions where selenium is plentiful developed fewer of certain cancers than residents of other areas, such as the northeast, where selenium is not abundant.

Also in laboratories where test animals received water containing extra amounts of selenium, the incidence of cancer development declined appreciably, particularly for liver and colon cancers.

Breast cancer causes more deaths among women in North America than any other cancer. In fact, in the United States, breast cancer is responsible for more deaths among women between the ages of 40 and 44 than any other disorder. According to a number of investigators, diets high in fat content probably contribute to the development of breast cancer.

Dr. Weitzman, who is also Assistant Professor of Medicine at Harvard Medical School, said that unsaturated fats, such as those derived from plant life, may be even more damaging than saturated fats found in meat.

"Unsaturated fats are very susceptible to oxidation and yield some very reactive lipid peroxides as byproducts of this action," he said. "These peroxides are potent mutagens [agents that cause genetic changes] in a variety of different systems."

On food containing the artificial sweetener saccharin, health authorities require an accompanying warning that "use of this product may be hazardous to your health."

Dr. Weitzman said that saccharin acts as a promoter of bladder cancer in test animals. "It will not cause the cancer," he said, "but if an animal has already been exposed to a cancer-initiating substance, the saccharin will bring out the cancer more quickly."

He emphasized that in laboratory trials researchers gave the saccharin in very high doses over a long term.

Other studies have linked excessive alcohol consumption to increased risks for cancers of the colon and rectum. Some evidence also points to a danger of liver cancer.

When alcohol is consumed by someone who also smokes heavily, the threat of developing a form of cancer multiplies.

"One does not see much cancer of the mouth, larynx, or esophagus in people who just drink or just smoke," Dr. Weitzman said, "but when they both drink and smoke, one sees a very high rate of these types of cancer.

"It's possible that all the alcohol does is affect the cells so that the threatening agents in the tobacco smoke can penetrate deeply into the mucous membranes."

Although health professionals have recognized since ancient times that dietary habits can influence disease in humans, the question of the role of individual dietary components remains only partly answered. But enough evidence is at hand to guide dieters to act more cautiously. And that is a major step in the battle. ■

Using specially bred mice which cannot reject grafts, Dr. Sigmund Weitzman tries out agents, including substances found in the diet, to see if any of them can prevent normal cells in inflamed areas from becoming malignant.

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 42 No. 7 October, 1983

Searching for a Way to Stave Off Birth Deformities

Mapping blood vessels in limbs of a genetically deformed mouse might yield clues to how the abnormality developed.

No one is born perfect. In one respect or another every baby varies from the norm. The difference may be as slight as the presence of a mole or a birthmark. Although defects, few prove later to be handicaps.

Two to three percent of newborn infants, however, have a malformation that is a disorder of body structure. Deformities of the arms and legs are one of the most common types of birth defects.

Faulty genes, the basic units of heredity, account for many malformed infants. Others stem from abnormal development of chromosomes, the thin strands of gene-carrying material found in the nucleus of every cell. And birth disorders can also result from some unwitting action. The mother during pregnancy, for example, might have taken a drug which also affected the fetus.

Although several different causes for birth defects have been identified, many remain unexplained.

With funds from the National Institutes of Health, two MGH specialists, Drs. David J. Zaleske and Lewis B. Holmes, are tracing the course of development of birth defects in order to shed more light on how they arise.

Dr. Zaleske is a pediatric orthopedist. Dr. Holmes heads the hospital's Embryology-Teratology Unit, which focuses on deformities present at birth.

In their studies of special mice that carry a destructive gene, the investigators found blood vessel abnormalities in areas where bone had failed to develop. And in breeding this type of mice, the researchers discovered that the blood vessel problems in the embryos preceded the limb deformities.

During the past few years a number of physicians have hypothesized on

(Continued on Page 4)

Pneumonia: A Disease Still Feared

Cancer, heart disease, kidney failure, chronic obstructive lung disease...

While a patient's death certificate customarily spells out what ailed him, the primary diagnosis does not always explain what killed him.

As diverse as the maladies may be, in the end they often share a common denominator. In each instance, the actual cause of death may represent a form of the same affliction: pneumonia.

Once the most common cause of death in the United States, pneumonia yielded to newly developed drugs in the 1930s. Penicillin reduced the death toll from pneumococcal pneumonia, the most prevalent bacterial form, from about 40 percent to less than 10 percent.

Today, however, pneumonia still ranks as America's fifth leading killer. Each year, it claims more than 80,000 lives. Ironically, lifesaving advances in the treatment of a number of disorders impair the body's ability to ward off foreign organisms, and this unavoidably contributes to lung insults that can prove fatal.

"As many as a quarter of healthy individuals carry pneumococcal bacteria in their throat," said Dr. Paul D. Goldenheim, Director of the Pulmonary Clinic and the Pulmonary Function Laboratory in the MGH's Ambulatory Care Center, "but the body's immune system normally keeps things in check. Also, in most individuals the bacteria are not aspirated into the lungs."

Even if the organisms slipped past mop-like structures [cilia] which line the bronchial tubes to drive out any

(Continued on Page 2)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206

Martin S. Bander	*Editor*
Myron H. Daniels	*Assistant Editor*
Doris G. Schreckengaust	*Copyreader*

EDITORIAL BOARD

J. Robert Buchanan, MD	*General Director*
Kurt J. Isselbacher, MD	*Research, Medicine*
Paul S. Russell, MD	*Surgery*
Ronald A. Malt, MD	*Surgery*
Roger H. Sweet, MD	*Utilization*
Stanley Bennett	*Photography*
Robert J. Galla	*Designer*

EDITORIAL:

Re McLean: Assurances or No Sale

In recent weeks the news media have reported frequently on the proposed sale of McLean Hospital by the MGH. At the outset, we would like to emphasize that the discussions with the Hospital Corporation of America (HCA) are still in a preliminary stage. Indeed a committee appointed to advise the Dean of Harvard Medical School about the concept has not yet issued its report.

In the meantime many of the news articles and editorials have expressed concern about the possibility of selling a distinguished nonprofit, psychiatric institution to a for-profit hospital chain.

We understand and share these concerns. Legitimate questions are being raised about a number of issues: Would the very fabric of an academic institution be permeated by the "taint" of capitalism? Would patient care, teaching, and research suffer? What would happen to academic freedom? Would such a sale set an unfortunate precedent? If economic factors became untenable, would a for-profit chain compromise excellence, or perhaps sell McLean to less scrupulous management? Would a for-profit chain continue to provide free care for the medically indigent?

In one form or other, these are questions we have asked ourselves since HCA initiated negotiations several months ago. First, the very thought of selling McLean, cofounded with the MGH in 1811, is a wrenching one. However, there exist major problems in financing simultaneously the replacement of obsolescent plants at both McLean and MGH at the very time Massachusetts hospitals are being squeezed by state regulations. The MGH itself has raised thus far only half the $114 million it needs for its own Capital Campaign. This then in brief is the background that impels the MGH even to consider the sale of McLean.

Let's jump ahead to the question of precedent. Although we believe we can fashion a creative contract, it may not be replicable for many other institutions. Surely we would advise other hospitals to think through as carefully as we are any offers that may be tendered them.

We have satisfied ourselves that in the HCA we are negotiating with an outstanding firm that tempers the dollar sign with a sense of fair play. While HCA is clearly not in business to lose money, we are convinced that to HCA McLean with its ties to MGH and Harvard Medical School represents prestige. As a consequence, officials of the huge hospital chain seem to be prepared, if need be, to operate the hospital without regard to profit. We want written assurances to protect McLean for all time against the type of negative possibilities enumerated here. For this reason we are painstakingly negotiating each issue. If we succeed, MGH, Harvard, and HCA will together have fashioned a creative way of dealing with future uncertainties. The beneficiaries would be McLean and its patients and the MGH and its patients. If we cannot be satisfied that the needs of McLean, MGH, and Harvard Medical School have been appropriately addressed, we will terminate negotiations.

Weakened Immunity Poses Lung Threat

(Continued from Page 1)

dangerous contaminants, certain white cells [macrophages] stand guard in the lungs to gobble up foreign particles (*MGH News*, November 1982 and March 1983).

When the immune system is weakened by illness, general debility, or the use of drugs to overcome an affliction, such as cancer, the possibility of serious lung problems mounts.

Pneumonia is an uncontrolled growth in the lung of an infectious agent which can both inflame the organ and infiltrate the lining of the airways, causing the production of mucus. As that sticky substance blocks the air sacs in the lungs, oxygen has a harder time reaching the blood. Without oxygen, the body's cells cannot function.

The infectious agent may be bacterial, viral, or a form of mycoplasma (*MGH News*, February 1970), an organism with growth characteristics of both a bacterium and a virus.

In addition to affecting people in poor health, pneumonia tends to be most prevalent among children with a still immature immune system and people over 50 whose immunologic defenses are waning because of age.

Dr. Goldenheim said patients with bacterial pneumonia rather than viral or mycoplasma pneumonia usually feel sicker, run a higher fever, and have a cough that produces greenish, yellowish, or rust-colored sputum. Occasionally, a bluish cast on the lips and nails may develop, leading to supportive treatment with oxygen.

Penicillin remains the drug of choice for pneumococcal pneumonias. In patients allergic to that medication, another antibiotic, erythromycin, is usually effective.

Some six years ago, a vaccine also became available to protect against 14 types of pneumococcus which cause about 80 percent of all pneumococcal pneumonias in the country.

Dr. Goldenheim described this vac-

Photographs: Pages 1, 4 (upper), 5 (lower), Myron Daniels; p. 3 (upper), courtesy of Dr. Daniel C. Shannon; (lower), courtesy of Dr. Lawrence J. Kunz, Dr. Robert Schooley, and Sarabelle Madoff; p. 4 (lower), courtesy of Colleen Kigin; p. 5 (upper), courtesy of Dr. David J. Zaleske; p. 6, courtesy of Dr. W. Allan Walker; p. 7, courtesy of Dr. Martin Stern; p. 8, courtesy of Michael Williams.

Prominent exposure of this 2-week-old baby's rib cage reflects breathing difficulties caused by lung-stiffening pneumonia that stemmed from a chlamydial infection.

cine as particularly valuable to people who for one reason or another do not have a healthy spleen, an abdominal organ which performs important blood functions.

"The spleen is terribly important in clearing so-called encapsulated bacteria, and the pneumococcus is the most common of those," said Dr. Goldenheim. "A pneumococcal infection is potentially devastating to the patient without a spleen."

Sickle cell anemia, found principally in blacks, often destroys the spleen. Injuries in contact sports such as football can result in loss of the spleen. So can injuries in car accidents. Surgeons sometimes remove the spleen to treat a disorder.

Dr. Goldenheim termed viral pneumonias as generally milder and more self-limited than the bacterial types. In addition, in most instances no drug treatment is necessary for the viral patient.

While the disease is usually mild, exceptions include patients with severely compromised immune systems and those with severe underlying heart and lung disease. Such patients are more likely to suffer respiratory failure or other complications from the viral afflictions.

Viral pneumonia induced by influenza may sometimes be complicated by a secondary infection, an overwhelming bacterial pneumonia, usually involving staphylococcus.

Doctors recommend influenza vaccine for all individuals who would be at high risk for complications if they contracted the flu.

"Anyone who is more than 65 or who has a chronic illness such as cancer, heart disease, lung disease, or liver or kidney problems really needs the flu vaccine," said Dr. Goldenheim, who is also an Instructor in Medicine at Harvard Medical School.

Mycoplasma pneumonia develops most frequently among older children and young adults. It is common, for example, on college campuses. Most patients pass off the illness as a severe cold or bronchitis. Usually, the patients get better without special care. When treatment is indicated, erythromycin facilitates recovery.

To diagnose pneumonia, physicians rely on chest X rays for only part of the answer. The X ray will reveal the presence of the disorder and the extent of involvement. Bacterial pneumonias tend to consolidate in one or more lobes, or sections, of the lung while viral and mycoplasma pneumonias appear more patchy, more diffuse.

To distinguish the specific type of infection, doctors must turn to the laboratory to study sputum specimens. Occasionally, under unusual circumstances, a bronchoscopy (use of a special, lighted instrument to visually inspect airways leading to the lungs) and a lung biopsy (surgical removal of a tissue specimen) are performed to help pinpoint the cause of pneumonia.

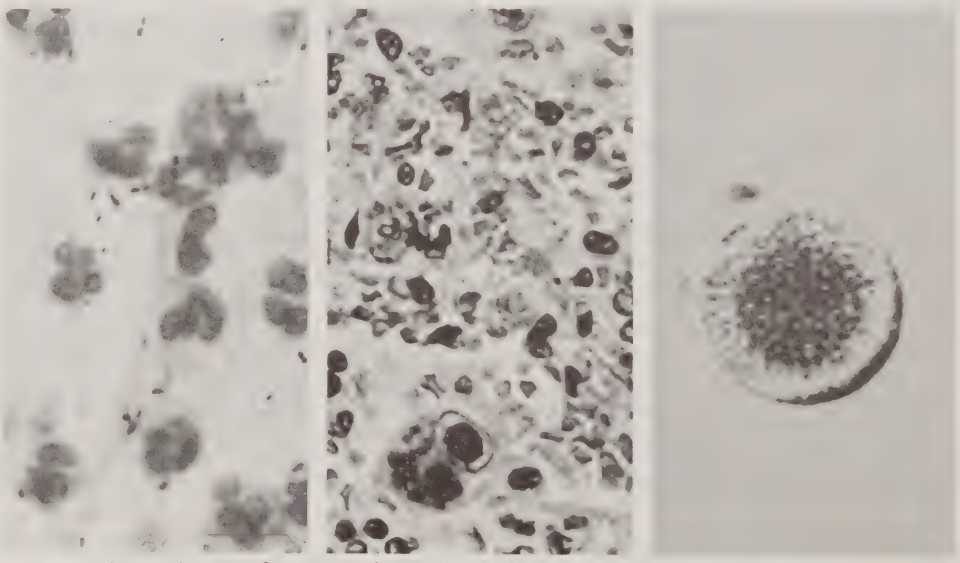
Often when a pneumonia appeared quite mild, physicians sought only to exclude the possibility of bacterial involvement. A specific diagnosis for viral or mycoplasma pneumonia usually did not seem necessary since these infections generally resolve themselves. One simply monitored the patient for any unexpected difficulties, e.g., too much stress on the cardiovascular system, a need for oxygen, or signs of respiratory failure.

Today, however, a specific diagnosis is becoming increasingly important because doctors are encountering in the general population pneumonias caused by agents not usually involved in this illness.

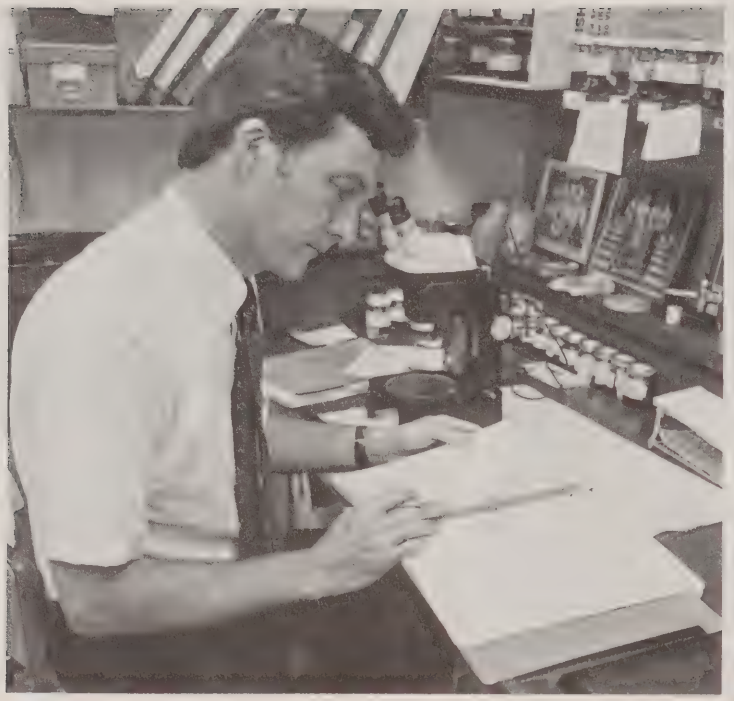
"We need to be alert to new epidemiologic patterns," said Dr. Daniel C. Shannon, Director of the MGH Pediatric Pulmonary Unit. "Today we have available more specific antimicrobial drugs to fight the problem.

"The pneumonias may be due to a

(Concluded on Page 4)



Microscopic specimens of pneumonia-causing infectious agents include, from left, pneumococcal bacteria, cytomegalovirus, and mycoplasma.



Dr. Lewis Holmes examines the family tree of mice whose inherited limb malformations are being studied in his laboratory.

Odd Blood Supply Linked to Defects

(Continued from Page 1)

examining malformed children that blood vessel disorders might have played a role in their plight. But no one had any idea whether the blood problem came first and the malformation second, or whether the two occurred at the same time.

The implication of the Zaleske-Holmes finding remains unclear, but as Dr. Holmes put it:

"Over and over, the general rule of thumb in medicine has been that once you understand how something happens, you have taken the first step toward being able to prevent it."

In their laboratory, situated in the MGH-affiliated Shriners Burns Institute, Drs. Zaleske and Holmes used 10

As Some Pneumonias Ebb, Others Arise

(Concluded from Page 3)

particular virus such as cytomegalovirus, a member of the herpes group; or the trachoma virus, Chlamydia trachomatis; or funguses, or pneumocystis organisms, which act like parasites."

Pneumocystis carinii pneumonia (PCP) is one of the principal illnesses which have befallen victims of AIDS (Acquired Immune Deficiency Syndrome) (*MGH News,* March 1983).

"PCP originally was thought to be a child's illness," said Dr. Shannon. "It was first recognized in premature babies in England in the late 1950s. We didn't see much of this pneumonia in the United States until chemotherapy [drug treatment] for various malignancies, such as leukemia, came along. PCP has since become a common complication."

Cytomegalovirus (CMV), known to have a suppressive effect on the human immune system, has been detected in nearly all patients stricken with AIDS. Under a grant from the National Institutes of Health, MGH infectious disease specialists are studying CMV's role in the syndrome.

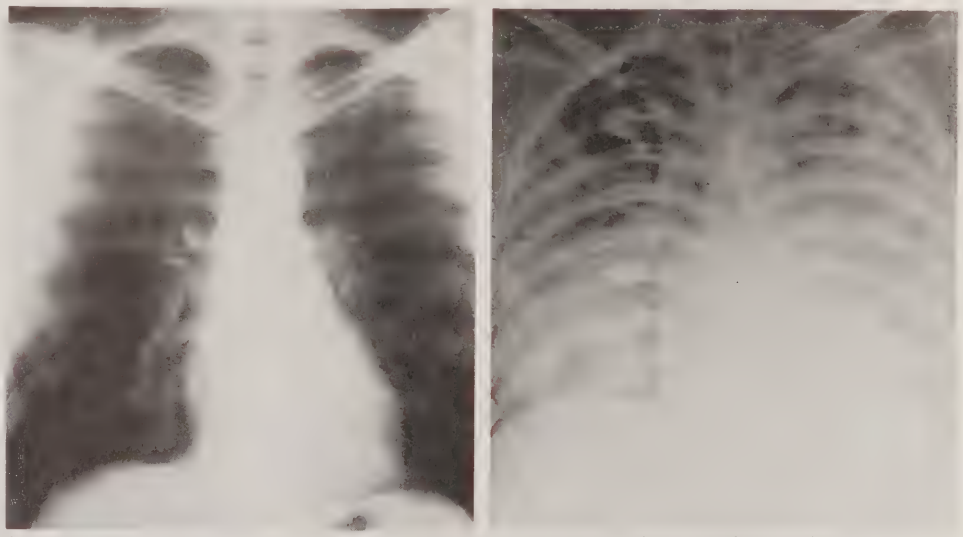
CMV has long been known to pose a grave threat to newborns, causing not only pneumonia but also brain damage ranging from hearing loss to retardation (*MGH News*, September 1977). And the virus is capable of increasing susceptibility of transplant patients to overwhelming bacterial pneumonia.

One microorganism that shares characteristics of bacteria and viruses also causes concern among pediatricians because of its ability to cause pneumonia and respiratory failure in infants. Dr. Shannon, who is Associate Professor of Pediatrics at Harvard Medical School and the Harvard-M.I.T. School of Health Sciences and Technology, referred to Chlamydia trachomatis (*MGH News*, October 1981).

This organism as a cause of pneumonia in infants was unrecognized 10 years ago. We now know that each year in this country 150,000 babies are born with chlamydial infections acquired from their mother, and pneumonia later strikes 30,000 of these infants. They respond well, however, to antibiotics.

Pneumonia is no less a problem in the 80s than it was in the 30s. While tuberculous, pneumococcal, and staphylococcal pneumonias are now controlled, other organisms have prospered.

Because of the mounting medical, economic, and psychosocial impact of pneumonia, pediatric and adult pulmonary and infectious disease specialists are finding themselves moving still farther into the forefront of health care in order to control and eradicate these "new" diseases. ■



X rays reveal, at left, a clear, normal chest and, at right, a chest stricken with pneumonia. Fluid and inflammatory cells filling air spaces in the lungs account for the cloudy appearance in the pneumonia picture.

healthy mice and 10 others that bore a gene called Dominant hemimelia (Dh), known to produce severe deformities of the hind limbs, absence of a spleen, and intestinal abnormalities.

Dr. Zaleske said that in animals with a severely malformed leg (tibia) he and Dr. Holmes consistently detected an absence of a blood vessel which normally goes to the leg. In the vessel's place was a persistent fine network of embryonic vessels which should have disappeared earlier to make way for bone development.

In another major finding, the two researchers also reported something unique about Dh-affected animals whose hind limb difficulties were minor. Each of these mice possessed an extra blood vessel not normally seen at all in the area where the bone should have formed.

In top photo, forceps hold main leg bone (tibia) of a normal mouse. In lower photo of another mouse, the tibia failed to grow because of an abnormal gene.

"...once you understand how something happens, you have taken the first step toward being able to prevent it."

The researchers found no vascular abnormalities in any of the mice which had not inherited the Dh gene.

The other phase of the MGH work, the breeding experiments, led to the development of a technique for predicting a limb deformity before it occurs.

The technique was made possible by taking advantage of the closeness on a chromosome of the Dh gene and a gene which makes an enzyme called peptidase-3, a substance which promotes a chemical reaction in the body.

Peptidase-3 comes in slow and fast forms, both normal conditions. In preparing a breeding experiment, one can determine that the Dh gene in one parent is close to a slow type of peptidase-3. In the other parent the particular chromosome under study would contain only normal genes near a fast type of peptidase-3.

"In the litter of such a pair," Dr. Holmes said, "if you looked on the eleventh day of gestation at the embryos' hind limbs when they were still immature and not yet deformed by the Dh gene, you would be able to detect the presence of the slow peptidase.

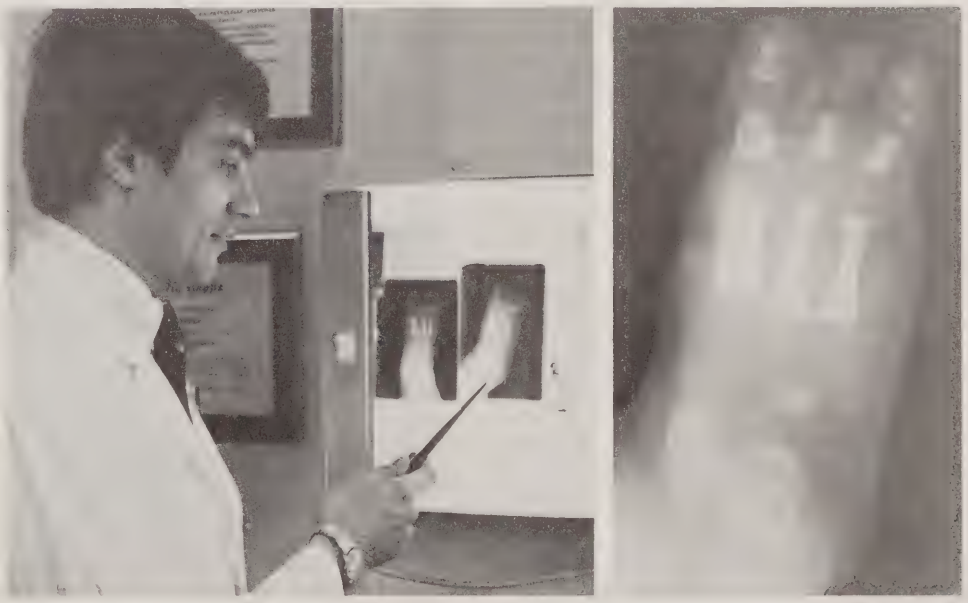
"Since the Dh gene is a dominant one, meaning that it is passed along by only one parent, there is a 50-50 chance of an embryo being affected. However, the presence in an embryo of the slow peptidase as a genetic marker provides 95 percent odds that this offspring will inherit the Dh gene. The effects of this gene cover a broad spectrum, ranging from a severe deformity to a mild one to no disability at all."

Learning 24 or 36 hours in advance that a limb may be deformed enables the researchers to gain a precise picture of the events leading up to any malformation.

The scientists will undertake this work in the next phase of the studies with the assistance of Dr. John T. Fallon, MGH Director of Cardiovascular Pathology and Chief of Pathology at the Shriners Burns Institute.

Dr. Zaleske, who is also Instructor in Orthopaedic Surgery at Harvard Medical School, would like to learn more about the specific types of blood vessel abnormalities that occur in the Dh animal because this limb affliction

(Concluded on Page 6)



Dr. David Zaleske views an X ray of a one-year-old child's foot which failed to develop completely (closeup at right). Through animal research, MGH investigators seek a broader understanding of the process which leads to such deformities.

Wartime Hostilities Helped to Explain A Major Illness

During World War II, certain Europeans who had been chronically ill before the hostilities began suddenly flourished.

Not until after the war ended did anyone begin to wonder about the almost abrupt health change.

The newly well citizens, it turned out, lived in pockets of the continent where fighting had destroyed wheat and other grain crops. As a result, bread, cereals, and other foods made with grain had fallen into short supply.

Studies revealed that a substance called gluten had made the patients ill, and its subsequent absence had enabled them to recover.

Gluten is a protein found in wheat, oats, rye, and barley. Some people inherit an intolerance for this protein. In such individuals, a component of gluten — gliadin — seems to be toxic to or destructive of mature intestinal cells in the body.

When healthy, the cells aid the digestive and absorptive process in the intestines. Even when crippled by the disorder, called celiac disease, the cells are replaced by new ones, but the successors are initially immature. Thus, the intestines are left with a severely limited capacity to digest food.

Suffering from celiac disease, this child was thin and weak at 22 months of age but showed dramatic improvement six months later after being on a gluten-free diet.

The patient becomes malnourished and loses weight. The malnutrition contributes to inability of the intestine to replenish itself. So, in effect, a vicious cycle has developed.

Celiac disease not only can retard growth but can also affect brain development if malnutrition sets in very early in life.

Dr. W. Allan Walker, who heads the Combined Division of Pediatric Gastroenterology and Nutrition at the MGH and at Children's Hospital Medical Center in Boston, said the effect "may not be overt mental retardation but mild, subtle difficulties such as inability to handle complicated problems later at school."

In some patients with celiac disease, intestinal malignancies may develop after 10 or 20 years, but this is rare.

The treatment of celiac disease, avoidance of all foods containing gluten, sounds simple enough, but all too frequently patients succumb to dietary indiscretions which can easily

Birth Deformities

(Concluded from Page 5)

has analogies to human limb defects at birth. The knowledge might add considerably to man's understanding of and ability to alter such human deformities. An even longer range benefit from controlling development would be availability of tissue for surgical intervention in severe accidents and tumors.

As for Dr. Holmes, an Associate Professor of Pediatrics at Harvard Medical School, he sees an opportunity to learn for the first time just how an abnormal gene can cause the absence of a bone.

Much controversy surrounds the rate of defective births in this country. Some groups claim that the number of babies born with physical or mental disabilities has doubled in the past 25 years. Other professionals contend that the definition of birth defects used in compiling the statistics was too broad.

These specialists added that rather than a big increase in new cases, the data may really reflect a rise in the number diagnosed. Half the birth defects that occur are not immediately apparent.

Ultrasound, an imaging technique that involves the use of high frequency sound waves (*MGH News*, January-February 1978), is being used increasingly to map structural development in fetuses during the second trimester of pregnancy.

For the most part, surgery after birth takes care of correctible defects, but reports in the medical literature describe experimental work on the fetus itself to help solve such problems as an obstructed urinary tract and an abnormal accumulation of fluid in the brain causing enlargement of the head (hydrocephalus). The surgeon removes the fetus from the mother to perform the operation and later returns the unborn child to the uterus.

Researchers have made much progress, particularly in the past decade, in preventing birth defects.

"Improved treatment of women with insulin-dependent diabetes is reducing their risk of birth defects to a significant degree," said Dr. Holmes. "If a woman alcoholic gives up drinking before she conceives, or as soon as possible afterward, she can decrease her risk of having children with defects.

"Spina bifida [abnormal development of the spinal cord] is now postulated to be preventable by giving the mother vitamin supplements before she conceives.

"And if a woman, herself successfully treated during infancy for PKU [the inherited metabolic disease phenylketonuria], went back on a special diet before she conceived, she could lower by 98 percent her risk of having birth-defective children.

All of which reinforces the argument that the more doctors learn about the causes of problems the more they can do to prevent them. ■

precipitate a relapse.

In addition, a multitude of foods contain ingredients derived from grains which the celiac patient must shun, and it is not easy to sort out these foods.

"Manufacturers are beginning to recognize that certain grains can be harmful and are using them to a lesser extent," said Dr. Walker. "And wary parents are looking closer at food labels. In starting infants on solids, for example, many mothers use rice cereals, which celiac patients can tolerate."

There has also been a sharp return to breast-feeding during the past decade. The number of mothers breast-feeding their babies has risen from 30 percent to an estimated 70 percent.

"Mother's milk provides the very young infant with some basic host defense mechanisms," said Dr. Martin Stern, a Pediatric Research Fellow at the MGH. "The longer a child is breast-fed the longer it is secure from foreign proteins such as are found in certain cereals."

Dr. Stern came from the University of Hamburg in Germany two years ago to work in Dr. Walker's laboratory, situated in the MGH-affiliated Shriners Burns Institute.

Evidence has mounted in recent years that celiac disease may be fading from the American health scene.

"The disease was once commonly discussed at hospital rounds," Dr. Walker said. "Everybody considered it when diagnosing the specific problem of patients suffering from an impaired ability of the intestines to absorb nutrients.

"Today, we discuss celiac disease much less often. Sometimes the attendance of foreign visitors at rounds is the only reason for mentioning the disease."

As many as 1 of every 200 residents in western Ireland suffer from celiac disease. In Sweden, the ratio is 1 in 950; in West Germany, 1 in 1,000; in Switzerland, 1 in 1,165. In contrast, Dr. Walker estimated that in the United States the disease affects 1 in 50,000 citizens.

Why the wide discrepancy? No one knows for certain, but changes in infant feeding practices, a withdrawal by food manufacturers of ingredients harmful to celiac patients, and more definitive labeling of foods are believed to contribute to the less frequent occurrence in this country.

Dr. Stern said that England and Switzerland, like the United States, have reported dramatic declines in frequency of the disease. But he said, "There are no firm data to conclude any correlations with any environmental factors. We don't see the disease waning in northern Germany or in Scandinavia. But the illness appears to have changed from the classic textbook description to a more mild appearance."

Wheat flour can be found in many, many processed European foods, he said, but although foods usually bear labels listing ingredients, enforcement is not as rigorous as in America.

"Some pharmaceutical companies in Europe use wheat flour in the manufacture of drugs when a powdery ingredient is needed," the doctor said. "Even lifesaving drugs may contain traces of wheat protein."

After six months on a diet that excluded gluten, this little celiac patient also lost a delicate, almost fragile, appearance and became robust.

Only children in Europe or in countries with a high population of European immigrants develop celiac disease.

When 19th century Boston opened its doors to large numbers of immigrants from Ireland, a high incidence of celiac disease prevailed. Each succeeding generation, however, became acclimated to new eating habits which caused a trend away from the disease. Today, that movement is toward supernutrition, including a high vitamin intake, more fiber in the diet, and a decrease in high-caloried foods.

"Resources are more limited in other countries," Dr. Walker said, "and traditionally wheat products have provided, in general, a reasonably good dietary intake at less expense. In our country people tend to lean more toward milk products as a better source of food."

Celiac disease requires lifelong attention. In adulthood, the disorder bears another name: nontropical sprue. Sometimes celiac disease goes undetected until the affected individual reaches the late 20s or 30s. During childhood the patient may escape the customary symptoms, such as diarrhea, weight loss, vitamin deficiency, distended abdomen, and anemia.

Once the patient embarks on a gluten-free diet, a feeling of well-being often develops after only two or three weeks.

Before implicating gluten in celiac disease, doctors usually prescribed bananas for such patients. Not only is this fruit nutritious, it also tends to soothe an irritated bowel.

Since the clinical picture of the disease has changed in the last 10 years, some investigators have proposed a screening test to detect the malady. One suggestion called for a test to spot and measure gliadin antibodies.

Dr. Walker, who is also Professor of Pediatrics at Harvard Medical School, said that establishing an unequivocal diagnosis of celiac disease involves a cumbersome procedure and any attempt to facilitate making the diagnosis should be pursued as far as possible. But in his view more investigation is in order.

"In the United States," he said, "so few people have celiac disease that to run a gliadin antibody test on every child who had diarrhea would be overkill." ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Misfortune Fails to Lessen Victim's Spirit

Forty-six-year-old Michael Williams is a man who perseveres.

Consider, for example, a trip that he made from his home in Hanover, Mass., to Falmouth on Cape Cod. He pedaled a bicycle the entire 67 miles.

Not bad for a middle-aged man with only one leg. In place of the leg he lost, he bicycles with an artificial limb which he designed.

Mr. Williams' right leg was amputated above the knee six years ago as the result of a road accident. But he made such a swift recovery that he has proved to be an inspiration to many other MGH patients who have also lost limbs.

An ardent sports buff who not only enjoys bike riding but also skis and plays golf, Mr. Williams frequently revisited the MGH's Rehabilitation Unit to comfort patients and to serve as an example of what determination and persistence could accomplish.

"I suppose I found it easier than most to recover mentally," he said. "With a wife and five growing children, I had just too many responsibilities to let anything in my own life interfere with their well-being."

Most of the patients he encountered on the Unit were in their 20s. Many had been in motorcycle accidents. "When one loses a limb at a young age," he said, "you can imagine how deeply depressed the individual can become. I tried to help out by explaining how I was able to deal with my own crisis."

Mr. Williams' accident occurred as he was bicycling to a tennis match. He said that as he swung into the driveway of the tennis club, he crashed into a night barrier ordinarily removed in the morning.

Treated initially at a local hospital, he was rushed to the MGH for specialized treatment of arterial injuries that stopped blood flow to his right leg. Doctors also feared that blood clots which had formed in the leg might break loose at any time and travel to a vital organ, threatening his life.

Surgeons performed a dozen procedures in a vain effort to save the leg. The amputation took place three weeks after admission, and Mr. Williams remained hospitalized for a total of three months.

Only two and a half months after his discharge, however, he was skiing at Vail, Colo., using outriggers (a type of crutch with a small ski at the bottom) to balance himself on his one leg.

Prior to his accident, Mr. Williams always relished being in shape. "I ran a lot, played a lot of tennis and golf, and rode my bike whenever I could," he said. "Today, bicycling occupies most of my leisure time because, like skiing, it permits a handicapped person to do almost as well as one who is physically normal."

He competes periodically in bicycle races, usually covering about 15 miles. He said that in a field of some 150 bikers he'll usually finish "in the middle of the pack."

To facilitate his bike riding, Mr. Williams, owner of a heating, ventilating, and air conditioning firm in Quincy, designed a special artificial leg and had it constructed by a local company.

"I found that the usual artificial leg, which is fine for normal everyday activities, is really a detriment on a bike," he said. "The prosthesis weighs 13 or 14 pounds and simply rotates with the pedal, lending no assistance in propulsion of the two-wheeler. In fact, because of improper alignment, the shoe often slides off the pedal."

To overcome this handicap, Mr. Williams employs a prosthesis that is basically a length of aluminum pipe, about one inch in diameter, with a hinge to serve as a knee joint. This leg is also fitted with a shoe, but it can be angled to sit squarely on the pedal.

The aluminum leg weighs only four pounds and, in Mr. Williams' estimation, permits a rider to transmit about 15 percent of the power that one would expect from a normal leg.

"I don't run across very many amputees who bike," he said, "but I can tell you that I am putting more mileage on my bicycle now than ever before."

He hasn't forgotten his other sports interests, however. Using his regular prosthesis, he still plays golf two or three times a week. ■

Only a few months after his leg amputation, Michael Williams skied at Sunapee, N.H., in a race sponsored by the New England Handicapped Sportsmen's Association.

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 42 No. 8 November, 1983

Pediatric Clinic Focuses on Major Lung Disorders

New Methods Permit More Precise Study Of Diabetes Control

When one considers that millions of diabetics stay alive through daily use of insulin, it becomes easy to recognize this drug's immense contribution.

But although insulin has clearly saved lives for 62 years, no one yet knows whether by lowering excess sugar, or glucose, in the blood the drug prevents or lessens the potentially serious complications of diabetes.

As many as 40 percent of diabetics develop at least mild signs of an eye condition called diabetic retinopathy. Three percent suffer severe loss of vision because of it.

Diabetes can produce kidney failure, nerve damage with consequent decrease of sensation in the extremities, and injury to blood vessels supplying the brain, heart, and legs.

Who will develop such secondary effects? When, and how severe will they be? These questions have gone unanswered largely because physicians lacked the tools to increase their understanding of the association between glucose and the complications of diabetes.

In recent years, however, such tools, to assure a precise measurement and tight control of blood glucose, have finally become available.

They take the form of a blood test that reveals a patient's average glucose level for the previous two months, a home method of accurately measuring glucose, and two types of insulin-delivery pumps, one implantable in the body.

With funding from the National Institute of Arthritis, Diabetes, and Digestive and

(Continued on Page 2)

"When we saw this young man almost four years ago, he was so sick he could have died any day. He was unable to walk more than 100 feet without stopping to catch his breath.

"During exercise testing, oxygen uptake by his lungs increased only twofold, just 20 percent of a normal increase."

Dr. Daniel C. Shannon, Chief of the MGH Pediatric Pulmonary Unit, was discussing a patient, then 17, whom we will call Fred. He was suffering from primary pulmonary hypertension, a form of high blood pressure which in other patients almost invariably leads to death within three years.

Admitted to the MGH, Fred underwent special tests which indicated that a lung operation might help, but surgeons ruled this out as too risky.

Dr. Shannon consulted with specialists in cardiology, radiology, and angiography (the special X-raying of blood vessels) about possible treatment.

"They suggested several medications," he said. "Since we feared the teen-ager would die if we didn't do something, we tried a number of drugs, and one worked. As far as I know, it had only been used once before in such patients."

After spending one week in the hospital, Fred continued his treatment entirely on an outpatient basis. Today, at 21, he has completed schooling and holds a full-time job requiring physical labor. To quote Dr. Shannon, "His oxygen consumption now increases tenfold with exercise, as it should."

Fred's remarkable recovery exemplifies what can happen when physicians with varied interests pool their talents to cope with a difficult illness.

With thoughts of patients such as Fred, MGH pediatric specialists on June 1 inaugurated a Respiratory Specialties Clinic. It centralizes care for children with any one

As the baby's mother watches, Dr. Lucienne Cahen examines 5-month-old Michael Silvio whose breathing pauses during sleep require special monitoring for his safety.

of a variety of breathing disorders.

The clinic brings together specialists for conditions such as cystic fibrosis, asthma, recurrent pneumonia, tuberculosis, and breathing irregularities during sleep.

The clinic performs pulmonary function testing and chest physical therapy and is open Wednesday mornings on the sixth floor of the Ambulatory Care Center (A.C.C.).

Dr. Allen Lapey, a member of the Pediatric Pulmonary Unit, supervises the clinic which Dr. Shannon said has three goals.

"First," he said, "by pooling the knowledge of six physicians with more than 100 years of combined experience in the pulmonary problems of children, we offer a strong diagnostic service.

"Second, this expertise assures ability to provide comprehensive, supportive care for

(Continued on Page 4)

MGH *News*

Published by the Massachusetts General Hospital, Boston, Mass. 02114 Telephone (617) 726-2206

Martin S. Bander — *Editor*
Myron H. Daniels — *Assistant Editor*
Doris G. Schreckengaust — *Copyreader*

EDITORIAL BOARD

J. Robert Buchanan, MD — *General Director*
Kurt J. Isselbacher, MD — *Research, Medicine*
Paul S. Russell, MD — *Surgery*
Ronald A. Malt, MD — *Surgery*
Roger H. Sweet, MD — *Utilization*
Stanley Bennett — *Photography*
Robert J. Galla — *Designer*

EDITORIAL:

The Loved One – the True Victim

Not too long ago an older person exhibiting marked signs of bewilderment and loss of reasoning ability was considered senile. That word still has considerable currency among lay people.

But a more specific term is gaining an accustomed and dreaded place in our vocabulary: Alzheimer's Disease (*MGH News*, September 1983).

Public service announcements, television documentaries, and newspaper articles have increasingly focused on this disease process. The reasons are obvious.

First, Alzheimer's is now known to afflict millions of Americans. Second, with the graying of America the disease is likely to become even more prevalent. Third, it devastates entire families.

A man or woman with Alzheimer's usually retains a sound body while the mind deteriorates before the eyes of the spouse. The loss of mental faculty grows profound. A 55-year-old man may have difficulty remembering his wife of 30 years. A 60-year-old may lose her way in her house of 35 years. A simple process like dialing a telephone number may become a staggering and terrifying chore. In effect the victim reverts to early childhood. For a husband or wife to have to treat a spouse like a 4-year-old destroys the meaning of marriage and the quality of life. In reality, the healthy loved one is the true victim of Alzheimer's.

The prevalence and nature of the disease are the terrible downside. The bright side is the growing awareness. Public concern will bring direct donations for research and will pressure Congress to appropriate more research funding.

Like the MGH, some hospitals have already opened units which treat and study the disease. Many more will follow.

Happily, these investigations come at a time when powerful new tools, such as genetic engineering (*MGH News*, April 1983) and monoclonal antibodies (*MGH News*, October 1982) have become available.

The ability to reverse the process or even cure Alzheimer's is unlikely to come overnight. Yet the constellation of resources brings considerable hope.

Will a Proper Blood Sugar Level Avert Diabetes Effects?

(Continued from Page 1)

Kidney Diseases, 21 medical centers in the United States and Canada, including the MGH, have launched a Diabetes Control and Complications Trial.

In a two-year pilot study involving some 250 volunteer patients, the centers will try to determine whether keeping blood glucose at optimal levels can avoid or minimize complications.

Dr. David M. Nathan, who codirects the MGH's recently opened Diabetes Research Center with Dr. Perry J. Blackshear, said two groups of patients are being formed for one study involving juvenile-onset, or Type I, diabetes.

These patients must have insulin supplied to them in order to survive. Their own bodies fail to make this hormone which is vital to the conversion of glucose into heat and energy. When the conversion fails to occur, the glucose builds in the blood.

One group of Type I patients will either wear an external, insulin-delivery pump or give themselves multiple insulin injections daily. In each instance, the patient, after receiving professional guidance, will adjust the dosage as required on the basis of frequently recorded blood sugar tests. The other Type I group will follow a standard injection schedule.

A second study at the Diabetes Research Center will assess the effectiveness of the implantable pump which was designed by Dr. Blackshear, then at the University of Minnesota, and a team there. This study will involve patients with adult-onset, non-insulin-dependent diabetes, referred to as Type II.

Unlike the external pump which delivers insulin at a steady but adjustable rate through a needle inserted into tissue, the implantable device, inserted into the chest, has only one rate of flow. However, it operates automatically and contains a reservoir that can hold a two-week supply of insulin.

Dr. Nathan said that studies of the new blood test, the self-glucose monitoring, and the insulin pumps will permit a much better assessment of their value in diabetes control, as well as their cost effectiveness.

"And the patients themselves, who will receive treatment without charge, will have intensive follow-up," Dr. Blackshear said.

Photographs: Pages 1, 3, 4, 5, 6 (lower), Myron Daniels; p. 6 (upper), courtesy of Dr. John D. Crawford

Drawings: Pages 7, 8, MGH Medical Art

An external pump worn by Technologist Edward Rose supplies him with a continuous low dose of insulin as he works in the Radiation Medicine Research Laboratory.

"If any complications develop, we should know about them much earlier than usual."

Even as these studies get under way, a synthetic form of human insulin made possible by genetic engineering is reaching the market to ensure an inexhaustible supply of the hormone.

Although the human insulin is described as purer and with fewer side effects than current insulins derived from the pancreas of cows and pigs, a major advance in purifying the animal hormone took place several years ago.

"The purity of the animal product in terms of insulin content rose from 92 or 93 percent to a level greater than 99 percent," said Dr. Joseph Avruch, Chief of the MGH Diabetes Unit. "This was achieved first in Scandinavia, then in the United States. The incidence of a variety of side effects that were not serious but often troubling diminished to a great extent."

Amid efforts to give diabetics longer, healthier, and happier lives, work is also being accelerated to learn the causes of diabetes.

Dr. Avruch said that in discussing juvenile-onset diabetes, so-called because it arises most often around the time of puberty, and adult-onset diabetes, which usually strikes after age 40, "we clearly are talking about two different diseases with different patterns of inheritance. They share a tendency toward high blood sugar and the same kinds of disease complications, but each type of diabetes has its own genetic basis."

Interesting data on this came from studies conducted in Britain on identical twins. One member of each pair had developed diabetes, and the question arose: What happened to the second twin?

"In well over 90 percent of instances where one twin had developed diabetes at age 40 or older, the second sibling also acquired the disease within three years," Dr. Avruch said. "This indicated for the first time that there was a tremendously powerful genetic component to adult-onset diabetes.

"Among twins with juvenile-onset diabetes, the second twin, in almost half the pairs, did not become diabetic during follow-ups lasting as long as 20 years. This indicated that while a strong genetic element was at work, it was not sufficient to cause diabetes but rather a susceptibility to the disease."

While little is known about the gene, or hereditary factor, causing Type II diabetes, a number of theories surround the cause of Type I.

Three or four years ago a child died two weeks after developing juvenile diabetes, and pathologists cultured a virus from his tissue. Investigators reinoculated the virus into laboratory animals and induced diabetes in them. Studies of a possible viral role are continuing.

Other researchers believe that a linkage exists between the Type I gene and another gene nearby which normally would protect against foreign organisms. The immune response, they think, may be abnormal with antibodies attacking rather than defending the insulin-producing islet cells in the pancreas.

Dr. Avruch said that scientists have found antibodies against the cells in an animal model for Type I and that suppression of this antibody production can block development of the disease.

Even after the affliction has set in, he said, treatment with a serum (antilymphocyte globulin) against certain normally protective white blood cells can in a third of the cases revert the animal to a nondiabetic state.

In view of these findings in animals, studies are under way in children to determine if a new immunosuppressive drug called cyclosporin A can fight juvenile diabetes when given during the first few weeks of the illness.

While the spotlight on diabetes focuses more on Type I, patients with the adult-onset form need not feel overlooked. Rep-

(Concluded on Page 4)

Christine Gauthier-Kelley, RN, teaches Michael Charest, a 13-year-old diabetic, how to obtain a blood sample for testing. Michael's parents look on.

Team of Specialists Consults on Every Pulmonary Patient

(Concluded from Page 1)

children and young adults with chronic breathing disturbances.

"And third, the clinic represents a new training ground for medical students, Residents, and Fellows in the field of pediatric pulmonary disease.

"In addition to getting the standard training in pulmonary physiology and diagnosis and management of chronic lung problems, it is also important that present and future physicians study the ever growing field of breathing-control disorders, such as prolonged apnea [temporary cessation of breathing], SIDS [Sudden Infant Death Syndrome], and hypoventilation."

The clinic is open to any child up to 18 years of age suffering from a respiratory difficulty. Private physicians refer all of the patients with cystic fibrosis and prolonged apnea and about half of those with asthma.

Although every staff member of the clinic has a special pediatric interest, all confer at length on each patient, regardless of the complaint, to evaluate the illness and determine care.

Dr. Lapey is also Director of the Cystic Fibrosis Center and Pediatric Allergy Clinic in the A.C.C. He and an associate, Dr. Kon-Taik Khaw, are among the senior staff in the Respiratory Specialties Clinic.

Dr. Lapey spoke of a chronic respiratory disorder (bronchopulmonary dysplasia) which sometimes affects premature infants who have required prolonged breathing support by a ventilator during the immediate period after birth.

"These babies will frequently develop a chronic lung condition that is extremely complex to manage and may require nutritional support as well as pulmonary skills," he said. "Until the new clinic opened, scattered parts of the institution saw such babies on a fragmentary basis."

Now patients have the opportunity to benefit from an organized comprehensive care program.

The clinic also means much to families with babies whose sleep is being monitored with an alarm device to protect them against prolonged apnea and, in some instances, an accompanying abnormally slow heartbeat.

The MGH home monitoring program (*MGH News*, January–February 1979), devised by Dr. Dorothy H. Kelly and Dr. Shannon, has now cared for close to one thousand babies. After initial hospitalization, each child has been seen again in a return visit to the MGH.

"The visits, however, might take place at any of several points in the hospital," said Dr. Kelly, who is Medical Director of the program. "We now hope to examine most of these children in the Respiratory Specialties Clinic."

Prolonged apnea, a cessation of breathing for longer than 20 seconds, is believed

From left: Using a stethoscope, Dr. Allen Lapey listens to the breathing of 14 on 12-year-old Jennifer Andella to check for possible allergies; and 9-year-old

Diabetes

(Concluded from Page 3)

resenting 90 percent of 11 million diabetics in this country, Type II patients can get along very well if they heed medical advice.

Dr. Avruch, who is also Associate Professor of Medicine at Harvard Medical School, said many Type II individuals take insulin. Others prefer oral drugs to control glucose levels.

"Actually, 80 percent of the patients with Type II should not have to take shots or pills," the doctor said. "It's entirely within their capacity to control their blood sugar by reducing weight and staying on a proper diet.

"The trouble is that changing the way one eats is a big adjustment, and patients don't like to do it." ■

Dr. David Nathan (right), Codirector of the Diabetes Research Center, discusses a variety of insulin pumps with a coinvestigator, Dr. John E. Godine, and Catherine Hurxthal, a staff nurse in the MGH Diabetes Clinic.

tephen Sodones; Medical Assistant Shaina Rubin-Rausch conducts a skin test
'Donnell undergoes a test to determine the breathing capacity of his lungs.

to be a major cause of sudden infant death.

The clinic also looks after children suffering from a hypoventilation syndrome which some people refer to as "Ondine's Curse" (*MGH News,* September 1979). From birth these children are unable to breathe adequately during sleep and turn blue unless they have ventilator support. While awake, they breathe normally.

Dr. Shannon and his staff are conducting a multicenter trial of a new respiratory stimulant in these patients.

Drs. Kelly and Shannon, and another colleague, Dr. Lucienne A. Cahen, also of the clinic staff, conduct extensive research on abnormal breathing patterns in infancy.

Asthma and recurrent pneumonias are excellent examples of conditions the origin of which may perplex family physicians and lead to consultation with the Respiratory Specialties Clinic.

An asthmatic attack occurs when muscles surrounding the lung's airways contract and restrict expiration of air from the lungs (*MGH News,* September 1980).

"Such an attack can be triggered by a variety of stimuli," said Dr. Denise J. Strieder, an MGH physiologist and member of the clinic. "The clinic frequently sees asthmatic children who are not clearly suffering from an allergy.

"Their asthma might turn out to stem from inhalation of toxic fumes or from a cooling of the airways due to exercise in a cold environment."

Recurrent pneumonias (defined as three or more attacks within two years) account for a large number of clinic patients. Interestingly, a common cause of recurrent pneumonias, usually in preschool youngsters, is asthma. For some reason, the child may not present the full symptoms of the illness; so it often goes unrecognized.

Dr. Strieder said pneumonias might also be due to congenital malformations of the lungs. In some children, recurrent pneumonias show an abnormal immune (disease-fighting) system because of either delayed development or true deficiency.

Bacterial pneumonia commonly appears as the initial symptom of tuberculosis, still a health problem although much less prevalent than before.

"The pneumonia sets in," Dr. Strieder said, "as the TB interferes with the normal function of a bronchial tube and hampers the ability of a lung to clear itself of any bacteria reaching there.

"Tuberculosis does not respond to antibiotics used for pneumonia. Special drugs have to be directed at the mycobacteria."

In discussing the new clinic, Dr. Lapey emphasized sensitivity of the staff to psychosocial issues that arise from living with a chronic illness.

"How the patient adjusts psychologically can influence his medical condition in a major way," the doctor said. "The well-adjusted patient copes far better and will lead a more productive life."

Dr. Lapey said that when speaking with families he and his associates stress that "we are interested first in the quality of life and second in the quantity of life. If you emphasize quality, you will also get quantity." ■

Helping a Child to Avoid Abnormal Height

When the average American adult tours a dwelling that dates from colonial days, he often must duck his head to pass from room to room.

Clothes tailored for a mature person in those revolutionary times might fit a 12-year-old today.

An increase in height has characterized human development for generations. Most parents assume that a son will wind up taller than his father and a daughter taller than her mother.

But little in life is absolute. Of every 10 children in the United States, one frets over abnormal stature.

Some 1,800,000 children fall below the third percentile in predicted adult height – less than 5 feet 4 inches for males and 4 feet 11 inches for females.

At the other end of the growth scale, excessive height also causes concern, especially among girls whose early development indicates an eventual height exceeding 5 feet 11 inches.

For many youngsters whose growth lags or spurts, early medical intervention can help. For others whose problems are especially complex, specialists still search for solutions. But inroads are being made.

Less than two years ago, the *New England Journal of Medicine* published details of a new treatment for precocious puberty, a childhood disease resulting in short stature. Today, medical specialists throughout the world agree that no other approach offers as much promise. Scientists hope the treatment may one day extend to other growth disorders.

In precocious puberty, sexual maturity inexplicably begins in very early childhood instead of around the age of 11 in girls and 12 or 13 in boys.

Although a growth spurt normally accompanies puberty, a permanent halt in growth soon follows. Thus, if puberty comes too early, growth also will cease too early. Approximately one half of girls with the disorder fail to attain an adult height of 5 feet. The disease occurs six times more often in girls.

To treat precocious puberty, physicians delay puberty with a drug which is a derivative of naturally occurring gonadotropin releasing hormone (GnRH). Produced in the hypothalamus of the brain, GnRH enables the pituitary gland to make hormones called gonadotropins. These, in turn, stimulate the testes to produce the

(Continued on Page 6)

Growth Disorder Yields to New Drug

(Continued from Page 5)

male sex hormone testosterone and the ovaries to produce the female hormone estrogen.

The blocking agent, more powerful than GnRH itself, was codeveloped by Dr. William F. Crowley, Jr., of the MGH's Vincent Research Laboratories and colleagues at San Diego's Salk Institute and the Developmental Endocrinology Branch of the National Institutes of Health (N.I.H.).

"The drug has proven to be effective and reversible in more than 200 children treated in this country and elsewhere," Dr. Crowley said. "We have demonstrated that as these children are treated they outgrow their predicted height."

While insufficient time has passed to determine long-term side effects, the drug has been relatively free of significant short-term ones.

Success of the treatment has led to an N.I.H. grant of more than $750,000 to the MGH for five additional years of research.

Dr. Crowley expects that the puberty-delaying drug will also help children deficient in growth hormone. While precocious puberty accounts for the short stature in 1 of 5,000 short adults, growth hormone deficiency affects approximately 50 times the number.

The continuing studies will also explore possible uses for the drug in countering growth loss caused by other disorders such as cystic fibrosis, diabetes, kidney disease, etc.

"A child may lose a year or two of growth because of illness, but unfortunately puberty usually develops on time," Dr. Crowley said. "The new treatment may be able to hold off the puberty. We think the potential to enhance growth is tremendous."

While the timing of puberty serves as an important factor in growth potential, it should be realized that any major metabolic stress lasting for any significant period of time during childhood can impair growth.

Dr. John D. Crawford, Chief of the Endocrine–Metabolic Unit in the MGH Children's Service and Chief of Pediatrics in the Shriners Burns Institute, an MGH affiliate, described poor nutrition as the principal reason for short stature.

"Good nutrition is particularly important during the first year of life when a child ordinarily grows 10 inches," he said. "That's four years' worth of growth later on."

Dr. Crawford often encounters the same scenario as parents, in many cases from affluent families, bring a child to him to complain of short stature. By this time, the youngster has reached school age. Standing next to classmates, his growth status becomes more apparent.

"The patient usually is the youngest child in the family," said Dr. Crawford. "His parents already have begun to fight the battle of the bulge. The milk in the refrigerator has little if any fat in it. The meat could not be leaner. The parents lose track of the child who is trying to get enough calories to grow.

"He does not have an inch of fat, and that is what Mother Nature looks at when she decides the question of growth. Fat is stored energy. Fat is insulation. Skinny children are inefficient children. It takes more than 80 percent of all the calories we consume just to keep our bodies at the proper temperature."

Physicians agree that emotional stress also ranks high as a cause of slow growth, usually acting indirectly through interference with appetite but sometimes directly disturbing the body's secretion of growth hormone. Alleviating the stress often permits growth to resume.

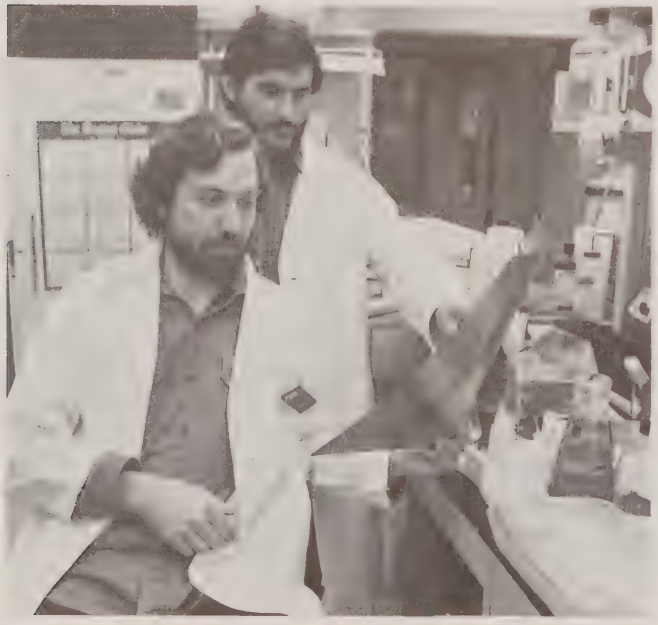
David Winterhalter, shown at age 3½ with his mother, was very short as a child. Treated for growth hormone deficiency, David, now 15, is passing his mother in height.

When asked to treat a girl destined to be very tall, Dr. Crawford, who is also Professor of Pediatrics at Harvard Medical School, first consults with the child. What height would she find acceptable? Would she be willing to undergo a treatment continuing for months and possibly including some unpleasant side effects?

Though seemingly strange, the treatment to brake growth calls for administration of estrogen, which in certain circumstances promotes growth.

The dosage and timing of its use determine the benefit to be gained. At puberty when small amounts of estrogen normally appear, the advent of the hormone is associated with a brief growth spurt before the growth plates are permanently fused. Larger amounts of estrogen accelerate the skeletal fusion process but meanwhile inhibit growth by blocking a liver protein called somatomedin. By giving the hormone at the appropriate time and in the correct dose, the doctor can stop growth at any point before its normal termination.

The reproductive system is just one of



In the Department of Molecular Biology, growth hormone researchers Richard Selden and David Moore, Ph.D., confer on a test analyzing DNA, the material of which genes are composed.

Weird Compulsive Acts Can Follow Obsessions

A patient coped with fears of self-injury by tying his hands before retiring each night.

Although the patient, a highly educated business executive, lived only two miles from his office, he often needed from 45 minutes to two hours to drive to work.

After traveling a short distance, he would circle the area and retrace the route. Not once, but again and again and again. He was obsessed with the idea that he may have caused an accident and that, without thinking, he had left the scene.

Occasionally, his circling of neighborhoods alarmed residents. Fearing that he might be planning a house break, they sometimes telephoned the police.

As often occurs in a patient with an obsessive-compulsive disorder (O.C.D.), severe depression was a component of the executive's illness. During the first few months of MGH treatment, this despair yielded to a tricyclic antidepressant. At the same time, behavioral therapy slowly paid off. The patient experienced long periods without further obsessions or compulsions.

No one can explain his irrational behavior. Indeed, O.C.D., which occurs in less than 2.5 percent of psychiatric patients, is probably the least understood of all the major psychiatric syndromes.

"A physician might encounter no more than three or four patients with an obsessive-compulsive malady during an entire career," said Dr. Michael A. Jenike. *Director of the Inpatient Psychiatric Service at the MGH, Dr. Jenike also heads an Obsessive-Compulsive Disorders Clinic which opened at the hospital last January.*

"Various professionals were seeing one or two such patients without any consistent way of caring for them," he said. "So several of us decided to start a clinic where we could systematically evaluate people with O.C.D. and make sure that we at least tried every treatment likely to work.

"I think that the life of everybody we've treated and followed for a number of months has improved by at least some degree. Some successes have been dramatic."

Numerous studies indicate that O.C.D. patients tend to have above average intelligence, which only accentuates the mystery surrounding their strange rituals.

Some recent examples:

. . . A man, fearful that he was going to hurt himself, bound his hands every night before going to sleep.

. . . Before retiring each night, another man, obsessed about fire, checked his home furnace and all the doors in his house three or four times.

. . . A lady felt compelled to wash her hands over and over for up to 10 hours a day.

. . . On looking out a window, another woman counted to 10 as many as 50 times after seeing something . . . anything . . . move. Then she spent hours touching every spot in her room.

"These people are not psychotics," said Dr. Jenike. "They are otherwise completely rational. Their compulsions make no sense even to them, but they find that their actions do alleviate anxiety. Without following their impulses, they might build their anxiety to a full-blown panic attack, including a feeling of impending death. This could be accompanied by physical symptoms, such as heart palpitations."

Scientists described obsessive-compulsive symptoms around the turn of the century, but some 50 years elapsed before they recognized O.C.D. as an independent entity.

They had regarded O.C.D. symptoms variously as a manifestation of schizophrenia, an emotional illness characterized by a retreat from reality; Tourette syndrome, marked by jerking movements of the body; major depression, or an organic mental disease.

Today with identifiable signs of its own,

(Concluded on Page 8)

two mechanisms that determine adult height. The other is the genetic potential for growth. Doctors can offer little help to the child who lacks height because of short parents.

In the MGH Department of Molecular Biology, however, researchers are examining the genetics of growth. They hope to devise a treatment some day to promote the growth of very small people whose status may have resulted from some genetic flaw.

Only a few years ago, Howard M. Goodman, Ph.D., now Chief of the Molecular Biology Department, and colleagues at the University of California, San Francisco, collaborated to isolate the first gene coding for human growth hormone. More growth hormone-like genes have since been isolated and are under study.

The work involves scrutiny of how a growth hormone releasing factor made in the hypothalamus of the brain causes the pituitary gland to release growth hormone made there, and how this hormone instructs the liver to secrete somatomedin. This is the protein, rather than growth hormone, which directly stimulates bone growth. Blockade of somatomedin production is an important part of the reason why estrogen can be used to slow growth.

Investigators find growth hormone interesting to work with because they can easily assess its effect. Looking to the future, they say the principles guiding the present research on growth may eventually reveal the causes of various other genetic diseases. ■

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Many Obsessed Patients Respond to Care

(Concluded from Page 7)

each disorder can be ruled out, leaving O.C.D. as the diagnosis. Although depression is commonly associated with O.C.D., the basic nature of the illness can be determined by finding out which symptoms arose first.

"We try to treat the patients on an ambulatory basis alone, but about 10 percent do wind up with some inpatient care," Dr. Jenike said.

Each Tuesday, staff members of the O.C.D. clinic convene in quarters on the seventh floor of the MGH's Ambulatory Care Center to discuss treatment planning and the progress of research on new approaches in care.

The clinic staff consists of Dr. Jenike; William E. Minichiello, Ed.D., and Lee Baer, Ph.D., both clinical psychologists with expertise in behavioral therapy; and two psychiatric residents, Drs. Andrew Brotman and Donald Goff, who are actively involved in pharmacological research.

Behavioral therapy, the treatment of choice for most compulsive ritualizers of the washing and checking variety, utilizes techniques of exposure and response prevention.

The patient is deliberately exposed to whatever situation triggers a compulsion, such as dirt which might lead to repeated hand washing. Then with a therapist present, the patient resists engaging in the compulsive ritual.

"Over time, the individual's anxiety rises, reaches a peak, levels off, and then begins to wear itself out," Dr. Minichiello said. "Cooperation of the patient and significant family members is essential."

Other behavioral techniques are also used to give the patient better control over his thoughts and actions. "A high percentage of patients show significant improvement, and those gains are usually maintained years after treatment," Dr. Baer said.

Antidepressant medication also may be prescribed. In some depressed people, parts of the brain are deficient in a class of chemicals called amines, believed responsible for mood changes. The medication helps to elevate the level of these chemicals.

On seeing movement through her window, a woman counted repeatedly to herself, then touched everything in her room.

The clinic staff has conducted pioneering research on a group of antidepressant drugs called monoamine oxidase inhibitors (M.A.O.I.). The O.C.D. clinic most commonly uses the M.A.O.I. inhibitors tranylcypromine and phenelzine.

Dr. Jenike, who is also Assistant Professor of Psychiatry at Harvard Medical School, said patients suffering from severe anxiety or who have experienced full-blown panic attacks seem to respond to the inhibitors.

He told of a 22-year-old woman who for five years was obsessed by an idea that her food was impure. She ate less, lost weight, became housebound, and performed a weird daily ritual, touching her tongue to items in her home.

Aware of a history of panic attacks, Dr. Jenike prescribed tranylcypromine for the woman. Within days, her compulsion stopped, and she began to go out with a boy friend. A few months later, she married him and also obtained employment. Two years after that, with the doctor's permission, she stopped her medication so that she could bear a child. The O.C.D. did not recur. Four years have passed, and the patient remains in good health.

Other drugs used for O.C.D. sufferers include so-called anxiolytic (anxiety-reducing) agents such as diazepam (Valium). Dr. Jenike said, however, that while they generally are useful in lowering anxiety they do not specifically help against obsessions or compulsions.

There are exceptions, such as the anxiolytic drug alprazolam. Doctors used it successfully in treating the man mentioned earlier who kept tying his hands.

The O.C.D. staff avoids antipsychotic agents. Dr. Jenike said they help only very acutely disturbed patients and have a potential for substantial side effects.

When O.C.D. patients fail to respond to multiple methods of medical and psychological care, a surgical procedure called a cingulotomy is a final option.

Studies have demonstrated that tiny lesions made in the cingulum, a small part of the brain at the top of the head, can produce much improvement in patients. Complications are rare, and with modern techniques personality changes are avoided.

The O.C.D. clinic staff has provided care for about 50 people afflicted with obsessive-compulsive disorders. "I suspect that within a couple of years that number will double," Dr. Jenike said. "We will have a real opportunity to employ various treatments and gather vital data. That is how medicine progresses." ■

MGH News

Massachusetts General Hospital, Boston, Massachusetts Vol. 42 No. 9 December, 1983

Factor in the Brain May Be a Cause Of Hypertension

Approximately 20 percent of American adults suffer from high blood pressure, or hypertension, but less than one of every 10 such patients knows the reason why.

In about five percent of individuals the cause can be identified and the high blood pressure cured. In the remainder, treatment can normalize the pressure, and the damaging effects of the hypertension can be avoided.

For the past six years, Dr. Garner T. Haupert, Jr., a physician in the MGH Renal Unit, has sought to unravel the mystery surrounding so-called essential hypertension, essential meaning in medical parlance "cause unknown."

Working under a grant from the National Institutes of Health, the doctor has discovered a substance, as yet unnamed, and its mechanism of action which may one day explain why hypertension occurs in many individuals. These studies have been reported in part in the scientific journal *Proceedings of the National Academy of Sciences.*

Dr. Haupert describes the substance as nature's own diuretic (an agent which increases the body's excretion of fluids and salts). It originates in a portion of the brain called the hypothalamus, which controls such functions as sleep, temperature, appetite, and emotions.

When the kidneys fail to properly excrete sodium, a principal component of the common salt that we eat in our diet, the volume of sodium and water in the body increases, sending a distress signal to the brain.

The brain factor now under study goes into action to increase the kidneys' excretion of salt and thereby reduce the sodium and water volume to a proper level.

In promoting a favorable effect on the

(Continued on Page 2)

Study of Children Leads to a Way Of Predicting the Use of Drugs

A three-year MGH study has produced a formula for predicting whether young school children will later use cigarettes, alcohol, or drugs.

Such a prediction—possible at the group level with statistically significant accuracy—raises the prospect of warding off use of these substances through special education at a very early age.

The study involved testing 1,474 students in grades 7, 8, and 9 in 1969 and retesting them three years later when they were in grades 10, 11, and 12. The students were from four school systems in Greater Boston and most came from white, middle-class families.

The research, reported in the scientific journal *Contemporary Drug Problems,* represents only one component of a massive undertaking that has spanned 14 years to date and embraced some 15,000 pupils from grades 4 through 12.

Dr. Garner Haupert of the Renal Unit visited an Omaha packinghouse for five days to collect cattle brain tissue for his hypertension research.

In their initial testing of the 1,474 youngsters, the investigators, directed by Gene M. Smith, Ph.D., an MGH Psychologist, measured five so-called predictive psychosocial variables. One is a self-report of attitudes and behavior regarding obedience and conformity to limits placed on childhood behavior by adult society.

From answers to 33 questionnaire items, the study team judged whether the child complies with the expectations that parents and society in general have concerning children's behavior.

Such compliance was indicated by affirmative responses to statements like: "I feel guilty when I break a rule." "I would never dream of cheating." "Even when I don't like someone, I try to be polite." "My parents think I can be trusted." And "I follow the rules even when I feel like breaking them."

An antisocial attitude was reflected by the student's support of such statements as: "If I think I can get away with something I've done wrong, I usually try." "When rules and regulations get in my way, I sometimes ignore them." "Some people don't seem to trust me." "If I don't feel like doing something I'm supposed to do, I often put it off." Or "It isn't hard for me to lie if I think a lie is necessary."

Two other predictive variables are based on peer ratings of personality characteristics. One peer rating variable evaluated obedience and the other measured sociability.

Dr. Smith said that peer ratings in which each child in a homeroom rates the personality characteristics of each of the other homeroom members is rarely used in psy-

(Continued on Page 4)

MGH *News*

Published by the Massachusetts General Hospital,
Boston, Mass. 02114 Telephone (617) 726-2206

Martin S. Bander — *Editor*
Myron H. Daniels — *Assistant Editor*
Doris G. Schreckengaust — *Copyreader*

EDITORIAL BOARD

J. Robert Buchanan, MD — *General Director*
Kurt J. Isselbacher, MD — *Research, Medicine*
Paul S. Russell, MD — *Surgery*
Ronald A. Malt, MD — *Surgery*
Roger H. Sweet, MD — *Utilization*
Stanley Bennett — *Photography*
Robert J. Galla — *Designer*

EDITORIAL:

Three Leaders and Their Times

When Dr. J. Robert Buchanan became the eighteenth General Director of the MGH, many people commented that the Board of Trustees had chosen well for a very difficult time. Now in the second year of his tenure, Dr. Buchanan has clearly demonstrated his considerable grasp of hospital economics and governmental regulatory bodies. These are the two mighty external forces that push and shove hospitals these days. His understanding of these issues as well as the traditional ones involved in operating a hospital has kept the good ship MGH well on course.

In naming Dr. Buchanan, the Trustees were carrying out a tradition of matching the General Director to the era. A new history of the MGH (page 6) chronicles this fact. Spanning the 25 years between 1955 and 1980, the book describes the administrations of three General Directors. The first of the three was Dr. Dean A. Clark, who envisioned major changes. In fact one can argue that Dr. Clark was *not* in step with his times. In a number of ways he anticipated the 1970s. Like many prophets, he failed during his own administration to see the fulfillment of his visions. Some of them reached fruition a generation later.

In turn Dr. John H. Knowles led the MGH through a period when the hospital needed an infusion of spirit. A very public man, he lifted the MGH onto his shoulders and with a grunt heard 'round the world hurled it soaring toward the sun. At the same time he created a number of innovations. After the successful interregnum of Acting General Director, Dr. Benjamin Castleman, Dr. Knowles' successor moved quietly but firmly. Dr. Charles A. Sanders patiently developed new buildings, programs, and relationships. When his tenure ended, he had left behind a remarkable trail of achievements. Thus the success of the MGH in recent years traces to the energy and brilliance of its chief executive officers. And ultimately to the Board of Trustees who chose them.

Disrupted Enzyme Can Permit Blood Pressure to Rise

(Continued from Page 1)

kidneys, however, the brain substance can affect blood vessels adversely because of the way it works in our bodies.

"In doing its job," Dr. Haupert explained, "the substance inhibits an enzyme which is not only related to the kidneys' excretion of sodium but also lives in virtually every cell in the body, including the vascular, smooth-muscle cells that are responsible for proper tone of the vessels.

"The function of the enzyme, which is also known as a 'sodium pump,' includes driving sodium from the cells. Once inhibited, this pumping activity slows, and the sodium accumulates in the cells. When this happens, a second buildup develops in the cells: an accumulation of calcium ions which are known to stimulate muscular contraction. Such a clampdown on the blood vessels could raise blood pressure."

The action of the brain substance on the enzyme is analogous to what occurs when a patient suffering from heart failure receives digitalis or digoxin. Through inhibiting the sodium pump in the heart muscle cells, the drugs produce a beneficial effect on the failing heart by increasing the force of its contractions.

Scientists have carefully studied the enzyme, formally called sodium-potassium ATPase, and the presence of a naturally occurring diuretic substance has been suspected for some 20 years.

Since making his discoveries about the existence of the brain factor and its mechanism of action in 1979, Dr. Haupert and coworkers in his laboratory have been working to purify the substance so that its molecular structure can be determined and synthesis, or production, made possible.

"The major difficulty in the purification effort," Dr. Haupert said, "is that the study involves a substance which exists in exceedingly small quantities. To identify the structure of a molecule requires a reasonable amount of purified material."

Rather than collect the factor from blood or urine, the doctor went right to a more appropriate source. He spent five days in an Omaha, Neb., packinghouse, removing

---

Photographs: Pages 1, 3 (lower), courtesy of Dr. Garner Haupert, Jr.; p. 3 (upper), Myron Daniels; p. 4 (upper), courtesy of United States Department of Justice; p. 4 (lower), courtesy of United States Department of Health and Human Services; p. 5, courtesy of American Cancer Society; pp. 7, 8, MGH Archives

Drawing: Page 6, MGH Medical Art

hypothalamic tissue from cattle just slaughtered for beef. He brought home 120 pounds of the tissue preserved on dry ice.

In conducting his laboratory research, Dr. Haupert must also have animal kidneys.

"In order to learn the physiologic events that take place," the doctor said, "I have to inject the brain material into a living organ. Tests and measurements are subsequently made of the urinary salt and water content.

"Animals are absolutely essential to this kind of investigation because no equipment even approximates the incredibly complicated machinery of the body. Even the artificial kidney is a mere pittance of effectiveness and sophistication when compared to the mammalian kidney."

Dr. Haupert, a member of the Harvard Medical School faculty, emphasized that his study may hit a steel wall, but he believes the long-term outlook is promising.

"We've made steady progress in the purification effort," he said, "but how long the work will take no one can say.

"Afterward, organic chemists, the people whose business it is to determine how atoms are hooked up to make molecules, will be asked to define the structure of the brain material.

"Subsequent synthesis may not prove terribly difficult since the material has a low molecular weight. Once this step has been accomplished, all of the long laborious efforts would be over."

One could then set about developing an antibody to the brain substance. The antibody would make possible a diagnostic test (a radioimmunoassay) to determine the presence and strength of the naturally occurring diuretic in the blood of a patient with essential hypertension.

To perform such a test, technicians would mix the antibody with a radioactive tracer quantity of the brain material and combine these with a sample of blood from the patient. The antibody-tracer complex would seek out the brain factor in the blood sample and reflect the levels that are present.

Senior Research Technician Laimute Kormos adjusts flow rate on a chromatographic column used in purifying a brain substance implicated in essential hypertension.

The antibodies themselves might be useful in counteracting the factor's effects upon the body. By virtue of their specificity, the antibodies would likely cause few untoward side effects.

An ability to produce the brain factor itself might permit patients to gain the benefits of a needed diuretic without the side reactions now caused by synthetically made diuretics. Such reactions include a loss of potassium into the urine, an upset stomach, and sluggishness.

Thus, patients with conditions marked by excess body fluids, illnesses such as congestive heart failure, nephrotic syndrome (a type of kidney disorder), or cirrhosis of the liver with an abnormal accumulation of fluid in the abdominal cavity, might benefit from treatment with the natural diuretic substance.

Dr. Haupert also said that the secretion of substances that stimulate nerves in the central and peripheral nervous systems is related to sodium pump activity. Therefore, the brain factor may turn out to be a basic regulatory agent that plays a very important role in nervous system activity.

Hypertension can result from a narrowing of a renal (kidney) artery, any one of several kidney diseases, tumors in the adrenal gland causing overproduction of a stress hormone called norepinephrine, and an excessive output of cortisone due to a tumor or an abnormally large number of cells in the adrenal gland. Knowing the respective cause, doctors can attack each disorder.

"In studying essential hypertension," Dr. Haupert said, "we have gone all the way back to the very root of the hypertensive process, seeking to understand what causes high blood pressure in the vast majority of the people who have it. Such understanding may suggest many approaches in care. The most effective treatment for a disease state occurs only after you know what the problem actually is." ■

To evaluate the brain substance believed capable of raising blood pressure, scientists inject the factor into this functioning rat kidney and then measure the subsequent content of salt and water in the organ's urine.

Left photo shows leaves of the marijuana plant while right photo exhibits various paraphernalia used in smoking the material.

Tests Give Many Clues to Student Trends

(Continued from Page 1)

chology, but he pointed out that extensive and prolonged interactions among children allow them to acquire much information about the personal characteristics of each other.

"Human beings," he said, "spend much time observing, evaluating, and drawing conclusions about other human beings. Even the most transient interaction between two individuals tends to influence to some degree, and at some level of consciousness, the feelings, opinions, and conclusions each has regarding the other."

Another predictive variable used in the analysis is grade point average, the child's academic standing in school.

The fifth predictive variable measures cigarette smoking by having the student respond to such statements as "I don't think I will ever become a smoker" or, conversely, "Most of my best friends smoke."

Asked how the team could tell whether the answers were honest ones, Dr. Smith said he had previously collected data on peer ratings of smoking behavior. This unpublished information strongly validated the self-report ratings of cigarette smoking made by the students.

Using the results of the testing for the five predictive variables among the junior high school students, the investigators constructed a mathematical composite, a sixth variable if you will.

Dr. Smith said that each of the original variables provides some indication of the outcome regarding substance use in high school "but when we aggregate these variables into a single composite, we get a still better prediction.

"To some extent, the components of the composite are substitutable, one for the other, but each one also has some unique contribution to make to the more powerful composite predictor."

Retesting of the initial student group during their later years in high school produced the following results:

399 children did not use cigarettes, alcohol, or marijuana at any time during the three-year period of study.

336 avoided cigarettes, alcohol, and illegal drugs in junior high, *did* smoke cigarettes or drink in high school but *did not* become users of marijuana or any other illicit drug.

367 did not smoke marijuana in junior high but became infrequent users of marijuana in high school.

And 372 did not smoke marijuana in junior high but became *frequent* users in high school.

Originally funded by the American Cancer Society, the researchers at first investigated only predisposition toward use of cigarettes. In the third year, the National Institute of Drug Abuse took over the sponsorship, and the study gained new dimensions to include information about alcohol, marijuana, and other illicit drugs.

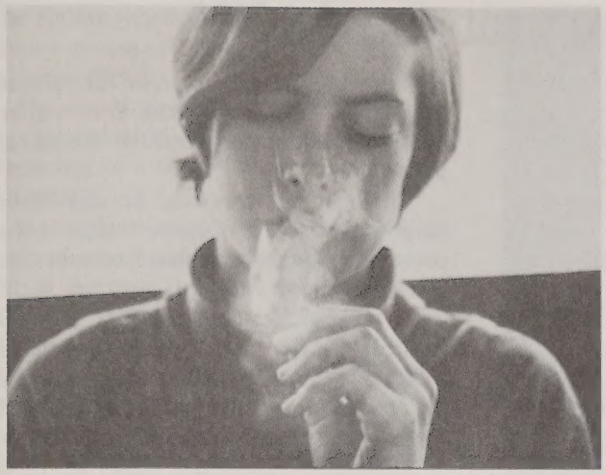
Dr. Smith said that one of the most interesting findings in the analysis is that the psychosocial measures predictive of escalation to cigarettes and/or alcohol from nonuse are the same variables that predict escalation to marijuana, and that "the stronger the junior high school psychosocial predisposition, the greater the high school escalation where it occurred."

This was clearly shown in the predisposition scores of the four groups just mentioned. The fourth group, those students who became frequent marijuana users in high school, scored higher than the third group. The third scored higher than the second, and the second ranked higher than the first group, i.e., those who avoided use of cigarettes, alcohol and illicit drugs throughout the three-year period of study covered by the present report.

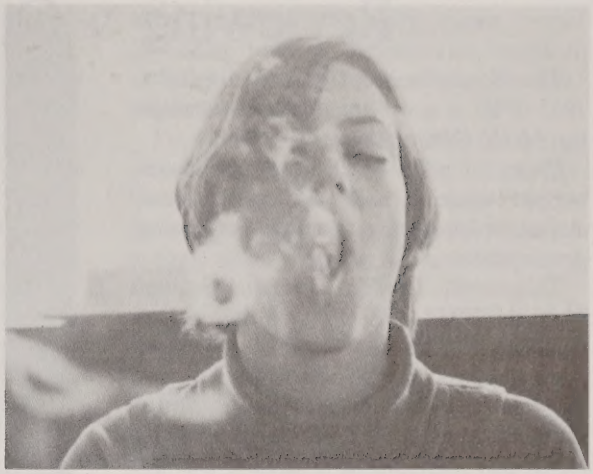
Thus, the four groups were found to be ordered the same way on predisposition as on escalatory outcomes, Dr. Smith said.

Another highlight of the study was the high degree of generality of the findings. "The same things we found for the males, we found for the females," the MGH psychologist declared, "and the same things we

Testing of 1,474 students revealed that several hundred began smoking cigarettes or drinking alcoholic beverages during their high school years.



For many the practice of smoking cigarettes might be averted if special courses on smoking hazards were given at an early age.



discovered about the 10th graders we found to be true about the 11th and 12th graders."

Many of the same students tested starting in 1969 were surveyed again in 1980 and 1981 by Dr. Smith and his colleagues.

"We wanted to see what their lives were like now that they were adults in their 20s," said Dr. Smith, who is also Associate Professor of Psychology in Psychiatry at Harvard Medical School.

"Were they married, and if so how stable was that marriage? What about their work habits and job performance? What was their psychiatric status as measured by a variety of scales? Had changes developed in any previously noted drug-use patterns? How well were they satisfied with themselves?"

This information is still being evaluated, but Dr. Smith said, "these newest analyses add to our conviction that there is an abstract concept (predisposition to drug use) that can be measured indirectly by measuring certain personality characteristics, attitudes, and behavioral traits at a very early age.

"This predisposition score is a strong indicator of the type and amount of licit and illicit substances likely to be used in the future."

Coauthors with Dr. Smith of the scientific report in *Contemporary Drug Problems* were Frederick T. Schwerin, a data analyst, and Frances S. Stubblefield, a computer programmer, both formerly affiliated with the MGH; and Charles P. Fogg, Ed.D., of Boston University, who also assisted in the collection and analysis of the data. ■

Taking the Heat Off Heartburn

The season is here when diets sometimes take flight and indiscretions replace the better part of valor.

Family gatherings traditionally highlight the holiday season, and the scenario invariably includes sitting around a table weighted down by a sumptuous meal. The temptation to gorge oneself is overwhelming.

For the individual who succumbs, the penalty often arrives within one to three hours: a feeling of fire under the breastbone.

One of the most common of all ailments, heartburn generally is little more than a temporary annoyance, but there is no missing its presence.

"It's a very real burning sensation," said Dr. Stephen E. Goldfinger, MGH Physician and member of the hospital's Gastrointestinal Unit.

"The feeling of extreme heat occurring alone actually is the most helpful factor in distinguishing heartburn from a heart attack. The person suffering a heart attack would generally experience a squeezing sensation in his chest rather than one of warmth."

Heartburn occurs when gastric juices rise out of the stomach into the esophagus, the tube which carries food from the mouth to the stomach. A mucous membrane protects the stomach lining from acid damage, but the esophageal tissue has no such armament.

The regurgitation may include not only acid but also pepsin, which is a digestive enzyme, and bile, a bitter alkaline liquid which also aids digestion.

Differentiating between heartburn and a heart attack can on occasion become a problem.

"The gastric juices may be so irritating to the esophagus," Dr. Goldfinger said, "that it may react by going into a spasm, a squeezing down. As a consequence, the person so affected may indeed get a pain much like that associated with a heart attack.

"While these instances are exceptions to the rule, they are important exceptions because the people with this condition are the worried ones we see at the hospital for diagnosis."

"Heartburn gives no advance warning, but it is not a condition that should terrify anyone."
—Dr. Goldfinger

A high-pressure zone in the wall of the lower esophagus normally prevents stomach contents from backing up, but when this area of muscular contraction (known medically as the lower esophageal sphincter, or LES) weakens, the gastric juices may slip by.

Many factors tend to reduce the pressure controlling these gates:

Distention of the stomach from overeating, and consumption of fatty, fried, or spicy foods, chocolate, garlic, onions, peppers, radishes, peppermint, coffee (both regular and decaffeinated), tea, and alcoholic or carbonated drinks.

Also, smoking, lying down too soon after eating, wearing a tight belt or girdle, and exerting abdominal muscles such as occurs while bending over and lifting a heavy object.

Certain drugs, such as tranquilizers or medicines used in treating asthma and irritable bowel disorders, can lower LES resistance.

Dr. Goldfinger said pregnant women

(Concluded on Page 6)

Reviewing a Quarter Century at the MGH

The Massachusetts General Hospital—1955–1980, a new book available through the MGH General Store at $22.95

Every 25 years or so the MGH pauses to take stock of itself and to chronicle events which have marked its continuing development.

This month, *The Massachusetts General Hospital—1955–1980* came off the presses of Little, Brown and Company, Boston. Through the contributions of 60 authors, the volume recapitulates in 397 pages the latest years in the life of America's third oldest voluntary, nonprofit hospital, dating from 1811.

The book spotlights the administrations of three General Directors, Drs. Dean A. Clark (1949–1961), John H. Knowles (1962–1972), and Charles A. Sanders (1972–1981). The account describes not only the many accomplishments of those periods but also the disappointments that inevitably fall upon every large medical care institution.

When Dr. Clark, a Rhodes scholar and graduate of Princeton University and Johns Hopkins Medical School, took the helm as the MGH's fifteenth General Director, he brought with him a new outlook on medical care.

"The hospital's services," he said "must be put to work for a broader range of the community's population than has heretofore been possible."

He proposed establishment of a group medical practice unit to make organized professional care available to ambulatory patients of all income groups and, at the same time, provide continuity of care for

Heartburn

(Concluded from Page 5)

seem particularly prone to heartburn because of a combination of increased abdominal pressure and higher levels of the female hormone, progesterone, which can weaken the LES.

"It is also known that many people with normal baseline LES pressure occasionally suffer heartburn," the doctor said. "This is because the sphincter may relax spontaneously for longer periods, thereby leaving the gates open longer."

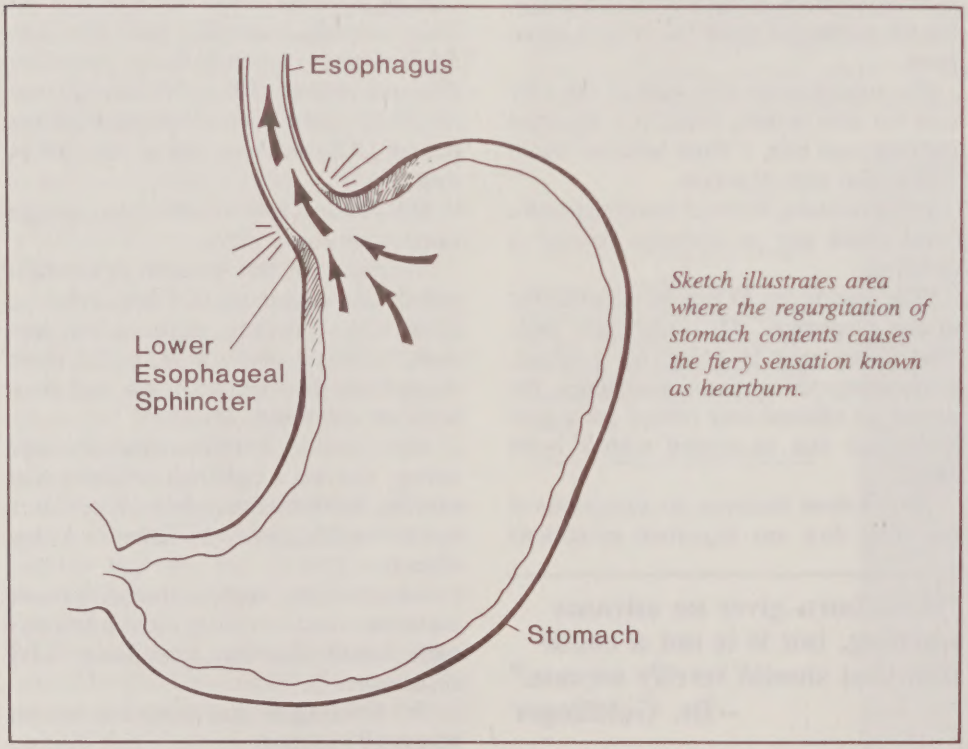
Heartburn sometimes occurs in patients suffering from a hiatus hernia (*MGH News*, April 1981). The hernia develops when the opening, or hiatus, in the diaphragm (the partition separating the chest and abdominal cavities) becomes too large and allows part of the stomach to slip up the esophagus into the chest.

"The hernia, however, may not be the cause of the heartburn," said Dr. Goldfinger, who is also Associate Dean for Continuing Education and Associate Professor of Medicine at Harvard Medical School.

"Barium X rays have revealed such hernias in so many symptomless individuals—up to 50 percent in some series—that it is evident the condition often causes no problem whatsoever. Any heartburn coexisting with the hernia usually turns out to be the result of a lax LES."

While the vast majority of hiatus hernias require no surgery, their repair frequently will resolve any heartburn problem because the techniques used also strengthen the sphincter.

For heartburn resulting from an occasional overindulgence at the dinner table, antacids, available over the counter in liquid or tablet form, constitute the treatment of choice. By neutralizing stomach acidity, these drugs reduce the tendency of regurgitated juices to irritate the foodpipe.



Sketch illustrates area where the regurgitation of stomach contents causes the fiery sensation known as heartburn.

Certain prescription drugs have become common heartburn remedies. Dr. Goldfinger said bethanechol seems to tighten the LES, and metoclopramide improves the flow of foods and liquids through the esophagus into the stomach.

Some physicians use acid blockers such as cimetidine. Introduced in the United States six years ago, cimetidine has proved to be extremely effective in the treatment of ulcers caused or aggravated by increased stomach acidity.

Mindful that a reflux, or backflow, of gastric juices into the esophagus brings on heartburn, people can adopt simple measures to prevent the condition in the first place:

- Shun those foods known to promote acid regurgitation and a weakening of the LES.
- Keep individual meals small, even if it means more than three sittings a day.
- Bear in mind that eating too fast increases the amount of air swallowed, thus contributing to distention of the stomach.
- Wait a few hours after a meal before lying down.
- Avoid tight belts or garments that press on the abdomen.
- Go easy on alcoholic beverages, and if you smoke, quit.
- Overweight? Shed those extra pounds.

"Heartburn gives no advance warning," Dr. Goldfinger said, "but it is not a condition that should terrify anyone. It has been estimated that about 35 percent of the adult population customarily have heartburn. Almost everybody has experienced it at some time in his life.

"Heartburn can last from a couple of minutes to several hours, but for most people an antacid can usually provide prompt relief." ■

the patient whether at home, as an ambulatory patient of the medical group, or in a hospital bed.

He also recommended the development, in collaboration with relevant community agencies, of a rehabilitation center at the hospital.

By today's standards, such objectives seem fundamental to effective health care, but at the time Dr. Clark proposed them, they were generally regarded as visionary, perhaps even diversionary. Dr. Clark's successors carried to fruition many of the proposals he had made.

During Dr. Clark's 12-year tenure, however, the MGH expanded substantially. A research building, nurses' dormitory, and the Warren Building, including five floors earmarked for the office practice of some 75 physicians, were added to the physical plant.

Between 1949 and 1960, MGH research quadrupled in expenditures to $5.2 million. Teaching programs in medicine also grew stronger as the size of the Resident staff rose from 100 to 140.

Dr. Clark's successors carried to fruition many of the proposals he had made.

After Dr. Clark stepped down because of poor health, the MGH trustees reached into the hospital ranks and chose as his replacement 35-year-old John Knowles, who had arrived 11 years earlier as an Intern. He was a product of Harvard College and Washington University Medical School, where he graduated at the top of his class.

Dr. Knowles, who had served as Chief of the Pulmonary Unit and Director for Medical Affairs, rose to the general directorship at a particularly sensitive time. The hospital was under a heavy strain because not only had Dr. Clark resigned but two legendary service Chiefs, Dr. Edward D. Churchill, in surgery, and Dr. Walter Bauer, in medicine, were nearing the end of their careers.

Dr. Knowles' impact on hospital morale, then precariously low, was simply incredible, according to David C. Crockett, a present Deputy to the MGH General Director. "Knowles turned this place around in a year!" said Mr. Crockett, who with the late Dr. Benjamin Castleman, former Chief of Pathology, and Sylvia Sutton, a writer and editor, helped to produce the new volume.

One of Dr. Knowles' most distinctive acts was to more than double the size of the MGH's most powerful medical body, the General Executive Committee.

By tradition its membership had been restricted to a small, select group of service Chiefs. Dr. Knowles insisted that each patient care service, as well as the Departments of Nursing and Social Service, have a direct representation. The result was a far more open and democratic structure.

Dr. Dean A. Clark

Other developments of the Knowles era included establishment of the Logan Airport Medical Station, Bunker Hill Health Center, and the Chelsea Health Center, ideas inspired by Dean Clark.

The Gray Building with the Jackson and Bigelow Towers represented the great building project of the era. They addressed urgent needs: new operating rooms, recovery units, research laboratories, medical care floors, a diagnostic radiology center, and other facilities.

Dr. Knowles resigned in 1972 to take on a new challenge as head of the Rockefeller Foundation in New York. In early 1979, he became terminally ill, returned as a patient to the hospital where he had spent 20 years, and died a short time later. He was 52.

Dr. Castleman took over in 1972 as Acting General Director until Dr. Sanders came on board. He did not have to travel far. The lanky Texan who had studied medicine at Southwestern Medical School and had become a cardiologist was serving as Chief of the MGH Catheterization Laboratory when the invitation came.

Many people later commented that Dr. Sanders was the right man for the times. The abundance of the sixties had given way to a new economic climate. In his first annual report, Dr. Sanders wrote:

"We are posed with the problems of applying existing knowledge to improving the delivery of health care without adding to costs."

The inflationary spiral of the decade proved overwhelming. The ability of the Sanders administration to at least moderate the rise in hospital costs was in itself a major achievement.

While restraining development in some ways, Dr. Sanders promoted it in others. As far back as 1964, the trustees had authorized planning for a structure to house radiation therapy. It was not until 1975, however, that the hospital dedicated the

(Concluded on Page 8)

Dr. John H. Knowles chats with a visitor.

News Office
MASSACHUSETTS GENERAL HOSPITAL
Fruit Street Boston, Mass. 02114

NONPROFIT ORG.
U. S. Postage
PAID
Boston, Mass.
Permit No. 57416

Ambulatory Center Meets Community Need

(Concluded from Page 7)

Cox Building, housing the MGH Cancer Center. The ambulatory center combines all forms of cancer treatment and research under one roof.

The MGH Institute of Health Professions, an idea of Dr. Knowles which offers degree programs in various health care specialties such as nursing, opened in 1980.

Dr. Sanders cut obstinately through red tape to win degree-granting authority for the hospital. He explained:

"We were sending a lot of people out of here with certificates that they had done this, that, or the other. They'd go to California, and that piece of paper wasn't worth a hill of beans. . . . I felt uneasy about the failure to standardize or meet certain criteria in the educational process."

Dr. Sanders' administration also built the nine-story brick Ambulatory Care Center which Dean Clark had longed for two decades earlier. No less committed to the concept of community care, Dr. Sanders had put this project at the top of his agenda early in his directorship. The Center opened last year.

Early in 1981, his last year as General Director, Dr. Sanders announced a $114-million fund drive, most of the receipts earmarked for the replacement of outmoded inpatient facilities.

Later in 1981, he also spearheaded a 10-year, $50-million-plus research contract between the MGH and Hoechst AG, an international pharmaceutical company. The funds created a new MGH Department of Molecular Biology, headed by a nationally renowned scientist, Howard M. Goodman, Ph.D.

Dr. Sanders left the MGH to become Executive Vice-President of E. R. Squibb & Sons at Princeton, N.J.

The past quarter century witnessed MGH growth in many ways, including prestige. The hospital's major achievements in medicine continued to mount at a rapid pace:

1962—The first successful replantation of a severed human limb

1964—Making practical the freezing of blood

1968—Telemedicine, the practice of medicine over two-way television

1971—Linking of DES (diethylstilbestrol) to a rare form of cancer in female offspring of women who took the drug to avoid miscarriage

1974—Development of photochemotherapy, a treatment combining light and drugs

During the 1970s, important progress was made on development of artificial skin at the MGH; Shriner's Burns Institute, an affiliate; and M.I.T. Successful human trials were reported in 1981.

Inescapably, the passing of time also saw the passing of many whose contributions helped the MGH to occupy the forefront of medicine. To name a few of the leaders who died between 1955 and 1980:

Drs. James H. Means and Walter Bauer, former Chiefs of Medicine; Edward D. Churchill, former Chief of Surgery; Joseph C. Aub and Fuller Albright, endocrine research; Paul Dudley White, cardiology; Chester M. Jones, gastroenterology; Robert R. Linton, vascular surgery; Joe V. Meigs, gynecology; James C. White, neurosurgery; Benjamin Castleman, pathology; Joseph S. Barr, orthopedic surgery; Wyland F. Leadbetter, urology; Henry K. Beecher, anesthesia; Laurence L. Robbins, radiology; Rita Kelley, oncology; and Stanley Cobb and Erich Lindemann, psychiatry. ■

Dr. Charles A. Sanders (center) and Dr. F. Sargent Cheever, then Chairman of the MGH Board of Trustees, conferring with members of the house staff